The Cost-effectiveness of Vaccination Against Lyme Disease

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Background: Vaccination against Lyme disease appears to be safe and effective; however, the cost per quality-adjusted life-year (QALY) gained with vaccination is unknown.

Methods: We developed a decision-analytic model to evaluate the cost-effectiveness of vaccination compared with no vaccination in individuals living in endemic areas of Lyme disease. Our analysis encompassed a 10-year time horizon including a 2-year vaccination schedule with an additional year of vaccine effectiveness. The costs and probabilities of vaccination risk, compliance and efficacy, and Lyme disease clinical sequelae and treatment were estimated from the literature. Health-related quality-of-life weights of the various clinical sequelae of Lyme disease infection were obtained from a sample of 105 residents from Nantucket Island, Massachusetts.

Results: Vaccinating 10,000 residents living in endemic areas with a probability of Lyme disease per season of 0.01 averted 202 cases of Lyme disease during a 10-year period. The additional cost per QALY gained compared with no vaccination was $62,300. Vaccination cost $12,600/QALY gained for endemic areas with an attack rate of 2.5% per season, and $145,200/QALY gained for an attack rate of 0.5%. Vaccinating individuals over an accelerated 2-month vaccination schedule improved the cost-effectiveness to $53,700/QALY gained. If a yearly booster shot is required for persisting efficacy, the marginal cost-effectiveness ratio increases to $72,700/QALY. The cost-effectiveness of vaccination was most sensitive to the Lyme disease treatment efficacy and assumptions about the persistence of vaccination effect.

Conclusion: Vaccination against Lyme disease appears only to be economically attractive for individuals who have a seasonal probability of Borrelia burgdorferi infection of greater than 1%.

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METHODS

THE MODEL

We developed a decision-analytic model to evaluate the cost-effectiveness of vaccination compared with no vaccination for persons living in areas of moderate to high risk of Lyme disease (Figure 1). The seasonal attack rate for the vaccine efficacy trials10,11 incorporated subjects living in the northeastern and upper midwestern United States, with yearly attack rates of approximately 1%, which roughly corresponds to the high to moderate risk areas in Figure 1. We constructed a Markov model to simulate a cohort of individuals through 10 seasons (Figure 2 and Figure 3).13 Each year (1 cycle length), an unvaccinated person faces a 1% chance of contracting Lyme disease. Persons with Lyme disease may or may not present with erythema migrans and may or may not present subsequently with disseminated disease. Dissemination was modeled according to the primary organ system involvement: rheumatological, cardiac, or neurologic manifestations. Vaccinated persons face a reduction in the probability of contracting Lyme disease. We assume that the course of Lyme disease among vaccinated persons is the same as that among unvaccinated persons. The model allows for full, partial, or no (1 shot) compliance with the 3-shot vaccination series with its concomitant protection evaluated in the context of the seasonal probability of Lyme disease. We assumed that partially compliant persons were only protected for the first season.10,11 Noncompliant persons were assigned the cost of 1 shot and received no benefit. Although the length of follow-up of the clinical trials used to evaluate the vaccine was 2 years, we assumed a persistence of vaccination effect of an additional year for fully compliant persons in our base-case analysis, and varied this assumption as a sensitivity analysis.

The model outputs were number of cases of Lyme disease, QALYs, and direct medical costs over a 10-year period. We also considered indirect costs in a sensitivity analysis. Incremental cost-effectiveness ratios for vaccination compared with no vaccination was calculated by dividing the additional cost by the additional benefit (measured in QALYs) of vaccination compared with no vaccination. We adopted a societal perspective and followed the reference-case recommendations of the Panel on Cost-Effectiveness in Health and Medicine.14 Costs and life-years were discounted at an annual rate of 3%. All analyses were performed using DATA software (TreeAge Software, Inc, Williamstown, Mass).

DATA

The probabilities and costs used in the model were estimated from the literature (Table 1). For each variable in the model, we assigned a best estimate to use in the base-case analysis as well as a clinically plausible range to use in sensitivity analyses.

Vaccine-Related Effects

The efficacy, compliance, and risk of adverse effects associated with vaccination were obtained from 2 recent clinical trials.10,11 The vaccination schedule included an initial dose at time 0, with 2 subsequent doses 1 month and 12 months later. Pooling the results from these trials showed efficacies of 62% for partially vaccinated (compliant) persons and 85% for fully vaccinated (compliant) persons. In our model, we assumed an efficacy of 62% for the first year, 85% for years 2 and 3, and no efficacy thereafter. The overall percentage of subjects in the 2 trials who received the first 2 inoculations was 98%, while only 83% of subjects received all 3 injections (73% in one trial; 92% in the other). The percentage of vaccine recipients who reported adverse effects was about 4% to 10% greater than that of placebo recipients. Typical adverse effects reported were pain or tenderness at the injection site and systemic symptoms of myalgias, achiness, fever, or chills. Symptoms lasted from 3 to 7 days.

Lyme Disease Sequelae and Treatment

In our model, 70% of patients who contract Lyme disease present with and are treated for erythema migrans.15-17 If this early treatment is successful, then disseminated Lyme disease will be prevented. Among patients who do not present with or do not receive treatment for erythema migrans or in whom treatment for early Lyme disease has failed, we assumed that they might then develop disseminated Lyme disease that manifests itself as arthritic, cardiac, or neurologic sequelae.12,18 Patients in whom initial antibiotic treatment for disseminated manifestations has failed were subsequently retreated with another 3 weeks of intravenous antibiotics. We assumed that a small fraction of patients who were retreated and in whom treatment failed developed a syndrome of arthralgias, fatigue, and cognitive difficulties that persisted for 5 years (modeled via a tunnel state).8,32 Persons are at risk for subsequent Lyme disease except for the small percentage who spend 5 years in the failure state.

Doxycycline and ceftriaxone sodium were the oral and parenteral antibiotics used in the model, respectively (Table 1). Doxycycline was used for patients with erythema migrans, first-degree atrioventricular block, Bell palsy, and arthritis. Parenteral ceftriaxone was used for patients with meningitis, radiculoneuritis or cranial neuritis, and arthritis resistant to an initial course of oral antibiotics. When there was a failure to respond to ceftriaxone therapy, individuals were retreated once more with a 3-week course. Treatment efficacies varied from 85% to 95% (Table 1). We also incorporated both minor and major reactions associated with antibiotic treatment in terms of cost.

Costs

The costs of management and treatment of Lyme disease were derived primarily from a previous cost-effectiveness analysis by Magid and et al14 and updated to 1998 US dollars using the medical care component of the consumer price index. The cost of the 3-shot series was estimated at $150 for fully compliant persons, partially compliant persons were assigned two thirds of this cost, and noncompliant persons were assigned one third of this cost. Persons experiencing adverse effects associated with vaccination, such as soreness, redness, and swelling at the site with myalgias and/or influenza-like symptoms, were assigned the
cost of ibuprofen, 400 mg 3 times daily, for 2 days and a visit to the physician in approximately 10% of cases. The cost of erythema migrans included the costs of an antibody test ($57), an office visit ($41), doxycycline for 3 weeks ($23), minor reactions to treatment (4% chance of incurring a cost of $81), and major reactions to treatment (0.01% chance of incurring a cost of $5933). Total medical costs associated with disseminated Lyme disease were based on previously published estimates. In a cost-of-illness study by Maes et al., when intravenous therapy failed in these individuals, they were retreated with 3 weeks of parenteral ceftriaxone at a cost of $3612. The annual cost of management of the post-Lyme disease fatigue syndrome included naproxen sodium therapy (500 mg twice daily) and amitriptyline hydrochloride, 50 mg, based on consensus opinion of 3 rheumatologists and tabulated using 1998 pharmacy costs at the Brigham and Women’s Hospital outpatient pharmacy. One of the assumptions in a reference case analysis is that morbidity costs are incorporated in the quality-of-life estimates. We challenged this assumption in a sensitivity analysis by incorporating morbidity costs from a cost-of-illness study by Maes et al.  

Health-Related Quality of Life

The health-related quality-of-life weights were estimated from a random sample of 105 residents from Nantucket Island, Massachusetts, an area with one of the highest incidences of Lyme disease in the United States (Table 2). Subjects rated a visual analogue scale that ranged from death (0) to perfect health (1) for each hypothetical clinical scenario. Each question was phrased in lay terms to approximate clinical manifestations of Lyme disease, including erythema migrans, facial palsy, heart block, arthritis, and meningitis, lasting for 30 days and a syndrome of fatigue, arthralgias, and difficulty concentrating, which was labeled as a post-Lyme disease “failure state” (Table 2). For example, the following descriptions were used to classify patients’ clinical state: “A large, red expanding rash for the rest of your life” (erythema migrans), “Your mouth droops and you drool” (facial paralysis), and “You have a swollen, painful knee...it is hard to walk” and “...joint and muscle aches...you forget things and cannot concentrate...” (failure state). Prior to administration, the questions were pretested for clarity among 16 subjects. Rating scores were converted to utilities (u) using a power transformation: $u = 1 - (1 - r)^3$. The estimated utilities were multiplied by the expected duration in each health state to estimate QALYs over a 10-year period.

SENSITIVITY ANALYSIS

We performed sensitivity analyses on all variables to assess the robustness of the results. Clinical probabilities, treatment efficacy, vaccine efficacy, and cost estimates were varied over a plausible range according to estimates from the literature. Utilities and seasonal attack rates were varied over a range that reflected the variation in the subjects’ responses. We also varied the cost of the vaccination series from $50 to $300 for a 3-shot series as well as an annual booster scenario.

RESULTS

BASE-CASE ANALYSIS

In the base-case analysis, which assumes an infection rate of 0.01 for Lyme disease per season, we predict that 202 cases of Lyme disease will be averted during a 10-year period for every 10000 persons vaccinated who live in an endemic area. This translates into an additional 0.7 quality-adjusted days (undiscounted) per person over the 10-year period, at an incremental cost of $62300/QALY gained and cost per case averted of $5300 for vaccination compared with no vaccination (Table 3).
SENSITIVITY ANALYSIS

Seasonal Infection Rate of Lyme Disease

The cost-effectiveness ratio of vaccination compared with no vaccination was sensitive to the probability of Lyme disease, with a seasonal infection rate of 2.5% resulting in a cost-effectiveness ratio of $12,600/QALY saved for vaccination. If the annual probability of Lyme disease were less than 0.50%, the incremental cost-effectiveness ratio was greater than $100,000/QALY gained (Figure 4). If a booster shot is required yearly and the efficacy persists for the 10 years of the model, the marginal cost-effectiveness ratio increases to $72,700/QALY. Because the persistence of the vaccination efficacy has not been demonstrated, we present a 2-way sensitivity analysis of the Lyme disease attack rate and the amount of time for which the vaccine is effective (Figure 4). Furthermore, a map of the United States based on level of risk for Lyme disease published by the American College of Immunization Practices demonstrates the variability in risk across the continent based on reports to the Centers for Disease Control and Prevention. Extrapolating the highest risk areas to seasonal probabilities of greater than 1%, moderate risk to between 0.5% and 1%, and minimal risk to less than 0.5%, one can estimate the range of incremental cost-effectiveness ratios by state (Figure 1).

Vaccination Effects

Using clinically reasonable bounds on vaccination efficacy, compliance rate, and adverse effect rate, the incremental cost-effectiveness ratio of vaccination ranges between $56,400/QALY and $88,700/QALY saved. If vaccination efficacy were only 0.43 for partially compliant persons, and 0.67 for fully compliant persons, then the incremental cost-effectiveness ratio increased to $88,700/QALY gained (Table 4). Using the base-case estimates for both vaccine efficacy and compliance results in a cost-effectiveness ratio of $51,900/QALY saved. Vaccinating individuals during an accelerated 2-month vaccination schedule (assuming that the 2-year efficacy could be achieved at 1 year) improved the cost-effectiveness of vaccination to $53,700/QALY gained.

Lyme Disease Prognosis

We varied the probability that a person infected with B burgdorferi would present with erythema migrans. Patients who do not present with erythema migrans fail to receive early treatment and thus are more likely to experience disseminated disease. As the probability of presenting with erythema migrans varied from 0.6 to 0.8, the incremental cost-effectiveness ratio for vaccination
varied from $46,400/QALY to $87,500/QALY gained. We also varied the probability of experiencing disseminated disease among patients whose conditions were not diagnosed, who did not present with erythema migrans, or who were not adequately treated. If there was only a 50% probability of dissemination, the cost-effectiveness ratio was $106,800/QALY gained. With 100% probability of dissemination, the incremental cost-effectiveness ratio was $49,500/QALY gained (Table 4).

Patients with erythema migrans who fail treatment are at risk of disseminated Lyme disease. If we decreased all of the Lyme disease treatment efficacies by 20% of their base-case estimates, the cost-effectiveness ratio of vaccination decreased to $18,800/QALY gained. Alternatively, if all treatments were 100% efficacious (and patients were 100% compliant with treatment), then the cost-effectiveness of vaccination increased to $301,900/QALY gained. Note that because we assumed that patients would be 100% compliant with their Lyme disease treatment, the base-case analysis is biased against vaccination.

Health-Related Quality of Life

Varying all quality-of-life weights over the interquartile range of responses yielded a substantial variation in the incremental cost-effectiveness ratio of vaccination from $39,600/QALY to $124,600/QALY gained. The model was most sensitive to the utility assigned to the small percentage of patients with persisting arthralgias and fatigue. As

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**Table 1. Model Estimates and Ranges**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Estimate</th>
<th>Range</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaccination</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Efficacy, 2 shots</td>
<td>0.63</td>
<td>0.43-0.74</td>
<td>10, 11</td>
</tr>
<tr>
<td>Efficacy, 3 shots</td>
<td>0.87</td>
<td>0.67-0.86</td>
<td>10, 11</td>
</tr>
<tr>
<td>Compliance, 2 shots</td>
<td>0.98</td>
<td>0.75-1.0</td>
<td>10, 11</td>
</tr>
<tr>
<td>Compliance, 3 shots</td>
<td>0.83</td>
<td>0.50-1.0</td>
<td>10, 11</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>0.06</td>
<td>0.01-0.20</td>
<td>10, 11</td>
</tr>
<tr>
<td>Persistence of effect, y</td>
<td>3</td>
<td>2-5</td>
<td></td>
</tr>
<tr>
<td>Lyme disease</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Attack rate per season</td>
<td>0.01</td>
<td>0.001-0.03</td>
<td></td>
</tr>
<tr>
<td>Erythema migrans</td>
<td>0.70</td>
<td>0.60-0.90</td>
<td>15-18</td>
</tr>
<tr>
<td>Dissemination</td>
<td>0.83</td>
<td>0.50-1.0</td>
<td>2, 9, 10</td>
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<tr>
<td>Arthritic sequelae†</td>
<td>0.73</td>
<td>0.50-0.75</td>
<td>2, 19-21</td>
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<tr>
<td>Cardiac sequelae†</td>
<td>0.07</td>
<td>0.02-0.10</td>
<td>20, 22-24</td>
</tr>
<tr>
<td>Neurologic sequelae†</td>
<td>0.20</td>
<td>0.04-0.22</td>
<td>18, 20, 25-27</td>
</tr>
<tr>
<td>Treatment efficacy</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Erythema migrans</td>
<td>0.95</td>
<td>0.80-1.0</td>
<td>18</td>
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<tr>
<td>Arthritic sequelae§</td>
<td>0.85</td>
<td>0.40-0.8</td>
<td>28</td>
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<tr>
<td>Cardiac sequelae</td>
<td>0.90</td>
<td>0.80-1.0</td>
<td>23</td>
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<tr>
<td>Neurologic sequelae</td>
<td>0.90</td>
<td>0.76-0.97</td>
<td>29-31</td>
</tr>
<tr>
<td>Risks with treatment</td>
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<td></td>
<td></td>
</tr>
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<td>Minor reaction, doxycycline</td>
<td>0.04</td>
<td>0.02-0.06</td>
<td>18</td>
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<tr>
<td>Major reaction, doxycycline</td>
<td>0.0001</td>
<td>0.0001-0.0005</td>
<td>18</td>
</tr>
<tr>
<td>Minor reaction, ceftriaxone</td>
<td>0.06</td>
<td>0.04-0.08</td>
<td>18</td>
</tr>
<tr>
<td>Major reaction, ceftriaxone</td>
<td>0.0001</td>
<td>0.0001-0.001</td>
<td>18</td>
</tr>
<tr>
<td>Costs, $</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vaccination series</td>
<td>150</td>
<td>50-300</td>
<td>Brigham and Women’s Hospital pharmacy</td>
</tr>
<tr>
<td>Vaccine adverse event</td>
<td>52</td>
<td>36-68</td>
<td>10, 11</td>
</tr>
<tr>
<td>Erythema migrans</td>
<td>124</td>
<td>87-161</td>
<td>18, 19</td>
</tr>
<tr>
<td>Arthritic sequelae</td>
<td>3610</td>
<td>2527-4693</td>
<td>18, 19</td>
</tr>
<tr>
<td>Cardiac sequelae</td>
<td>7627</td>
<td>14-163</td>
<td>18, 19</td>
</tr>
<tr>
<td>Neurologic sequelae</td>
<td>9733</td>
<td>6813-12-653</td>
<td>18, 19</td>
</tr>
<tr>
<td>Failure, short-term</td>
<td>3612</td>
<td>2528-4696</td>
<td>Assumed</td>
</tr>
<tr>
<td>Failure, annual</td>
<td>360</td>
<td>252-612</td>
<td>18, 19</td>
</tr>
</tbody>
</table>

*Probability of dissemination among patients not adequately treated for early Lyme disease.
†Probability of sequelae applies only to those patients experiencing disseminated Lyme disease.
‡Includes Bell palsy, meningitis, and radiculoneuritis or cranial neuritis.
§Encompasses total including efficacy of 0.7 for doxycycline and 0.59 for subsequent ceftriaxone.

**Table 2. Health-Related Quality-of-Life Adjustments**

<table>
<thead>
<tr>
<th>Clinical State</th>
<th>Utility</th>
<th>IQR Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema migrans rash</td>
<td>0.80</td>
<td>0.70-0.93</td>
</tr>
<tr>
<td>Arthritic sequelae</td>
<td>0.69</td>
<td>0.51-0.86</td>
</tr>
<tr>
<td>Cardiac sequelae</td>
<td>0.61</td>
<td>0.38-0.78</td>
</tr>
<tr>
<td>Bell palsy</td>
<td>0.61</td>
<td>0.36-0.81</td>
</tr>
<tr>
<td>Meningitis</td>
<td>0.52</td>
<td>0.27-0.73</td>
</tr>
<tr>
<td>Radiculoneuritis or cranial neuritis</td>
<td>0.60</td>
<td>0.36-0.79</td>
</tr>
<tr>
<td>Failure state (cognitive difficulty, arthralgias)</td>
<td>0.60</td>
<td>0.37-0.79</td>
</tr>
<tr>
<td>Myalgias, arthralgias</td>
<td>0.54</td>
<td>0.30-0.70</td>
</tr>
</tbody>
</table>

*Estimated from a sample of 105 residents of Nantucket Island, Massachusetts. IQR indicates interquartile range.
this utility was varied within its observed interquartile range (Table 2), the incremental cost-effectiveness of vaccination varied from $42900 to $97800.

**Costs**

The results were most sensitive to the cost of vaccination for the 3-shot series. If vaccination costs were only $50, then the cost-effectiveness ratio for vaccination was only $6900/QALY saved. If vaccination costs were as high as $300, then the cost-effectiveness ratio of vaccination was $145300/QALY gained. Varying the treatment costs of disseminated Lyme disease by 50% of the base-case estimates varied the cost-effectiveness of Lyme disease vaccination to between $52400/QALY and $72100/QALY gained. When we incorporated the indirect costs of Lyme disease, the incremental cost-effectiveness ratio for vaccination decreased by approximately $10000/QALY gained.

**Table 3. Base-Case Analysis**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No Vaccination</th>
<th>Vaccination</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lyme disease cases, No.</td>
<td>999</td>
<td>797</td>
</tr>
<tr>
<td>Discounted</td>
<td>878</td>
<td>682</td>
</tr>
<tr>
<td>QALY</td>
<td>99,927</td>
<td>99,945</td>
</tr>
<tr>
<td>Discounted</td>
<td>87,799</td>
<td>87,815</td>
</tr>
<tr>
<td>Cost of Lyme disease treatment, $</td>
<td>1,766,885</td>
<td>1,407,268</td>
</tr>
<tr>
<td>Discounted</td>
<td>1,551,108</td>
<td>1,202,222</td>
</tr>
<tr>
<td>Cost of vaccination, $</td>
<td>0</td>
<td>1,405,603</td>
</tr>
<tr>
<td>Discounted</td>
<td>0</td>
<td>1,393,637</td>
</tr>
<tr>
<td>Total cost of strategy, $</td>
<td>1,766,885</td>
<td>2,812,871</td>
</tr>
<tr>
<td>Discounted</td>
<td>1,551,108</td>
<td>2,596,859</td>
</tr>
<tr>
<td>Incremental C/E ratio, $/QALY</td>
<td>0</td>
<td>62,300</td>
</tr>
<tr>
<td>Incremental C/E ratio, $/case averted†</td>
<td>0</td>
<td>5300</td>
</tr>
</tbody>
</table>

* Outcomes per 10,000 persons vaccinated. QALYs indicates quality-adjusted years of life; C/E, cost-effectiveness.
† Costs and health effects are both discounted at 3% per year.

Little is known about whom to vaccinate against Lyme disease. In this study, we used established methods to evaluate the cost-effectiveness of Lyme disease vaccination. In an area with a probability of 0.01 per year of contracting Lyme disease, 202 cases of Lyme disease would be averted over 10 years for every 10,000 residents vaccinated, at an incremental cost-effectiveness ratio of $62,300/QALY saved and $5300 per case of Lyme disease averted. Because Lyme disease is usually nonfatal, the benefit of vaccination expressed in terms of QALYs reflects the relative impact on the patients’ time with symptoms.

The incremental cost-effectiveness ratio of vaccination compared with no vaccination varied substantially depending on the rate of endemicity of Lyme disease. The annual probability of contracting Lyme disease depends on host-parasite interactions, such as rates of *B burgdorferi* tick infection, cumulative exposure to tick-infested areas, the use of precautionary behaviors, and environmental factors such as seasonal rainfall and temperatures. In highly endemic areas, annual attack rates have been reported between 2.5% to 10%. Incidence rates collected from larger endemic areas, including the areas in 2 vaccine studies, showed annual rates averaging approximately 1%. Areas with lower attack rates (0.5%) raise the cost-effectiveness of vaccination to more than $100,000/QALY gained for a wide range of assumptions regarding the persistence of vaccine efficacy.

Our results were also sensitive to assumptions about the persistence of vaccine efficacy. Although the available clinical trials report efficacy for a 2-year time horizon, this is because of the 2-year timing of the vaccination series. Using a time horizon of only 2 years, Lyme disease vaccination cost $105,000/QALY gained. However, the incremental cost-effectiveness ratio decreased substantially to $29,600/QALY gained under the assumption that the vaccine effectiveness persisted for an additional 3 years.

Our results were also sensitive to the treatment effectiveness associated with Lyme disease. In our base-case analysis, we assumed that patients would be 100% compliant. Lower compliance with treatment would effectively lower the treatment effectiveness. If the base-case treatment efficacies were reduced by 20%, then the cost-effectiveness ratio of vaccination decreased to only $18,800/QALY saved. Alternatively, if treatment for Lyme disease (for both the early and disseminated states) were 100% effective and compliance with these treatments were 100%, then the cost-effectiveness ratio of vaccination increased to more than $300,000/QALY saved.

The results were also sensitive to the utility weights assigned to the Lyme disease clinical states. We compared our results with those of Nichol and coworkers. Although there were similar results for rheumatologic sequelae (0.68 vs 0.69), our utility weights were somewhat lower for erythema migrans (1.0 vs 0.80). The utility questionnaires were filled out by residents of Nantucket Island, which is highly endemic for Lyme disease. Nearly half of the 105 individuals who completed our questionnaire previously had Lyme disease. In the study by Nichol and coworkers, utility states were calculated via a time trade-off task by an expert panel. Our model was sensitive to the utility values varying between $38,500/QALY and $122,300/QALY, when the values were varied to within the 25th and 75th percentiles. Lower utility values would bias our analysis in favor of vaccination.

**Figure 4.** Incremental cost-effectiveness of vaccination vs nonvaccination in a cohort of individuals according to the yearly probability of infection and the length of efficacy of the vaccine. QALY indicates quality-adjusted life-year.
In a recent cost-effectiveness analysis, Meltzer et al.\(^2\) examined the Lyme disease vaccination in terms of cost per case averted. There were a number of differences between the two studies including Meltzer and coworkers'\(^2\) inclusion of indirect costs in the base-case analysis, higher treatment costs, and assumptions that included higher probabilities of dissemination, for example. Our cost per case averted was $5300 for a seasonal attack rate of 0.01, which was not too different from Meltzer and coworkers. Our results in terms of QALYs allow comparison with other preventive interventions.

Table 4. Sensitivity Analysis of the Cost-effectiveness Ratio of Vaccination

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base-Case Value (Range of Values Tested)</th>
<th>Cost-effectiveness Ratio, $/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy of vaccine</td>
<td>0.62 partial compliance/0.85 full compliance (0.74/0.86-0.43/0.67)</td>
<td>Biased Toward Vaccination</td>
</tr>
<tr>
<td>Vaccine compliance</td>
<td>0.98 partial/0.83 full (1/1-0.75/0.50)</td>
<td>57 000</td>
</tr>
<tr>
<td>Probability of presenting with erythema migrans</td>
<td>0.7 (0.6-0.8)</td>
<td>56 400</td>
</tr>
<tr>
<td>Probability of dissemination if no effective early treatment</td>
<td>0.83 (1.00-0.50)</td>
<td>49 500</td>
</tr>
<tr>
<td>Treatment effectiveness</td>
<td>See Table 1 (80% of base case, 100% effective)</td>
<td>18 800</td>
</tr>
<tr>
<td>Cost of vaccination</td>
<td>$150 ($50-$300)</td>
<td>6900</td>
</tr>
<tr>
<td>Cost of dissemination</td>
<td>See Table 1 (150% of base case to 50% of base case)</td>
<td>52 400</td>
</tr>
<tr>
<td>Lyme disease utilities</td>
<td>See Table 2 (25th percentiles to 75th percentiles)</td>
<td>39 600</td>
</tr>
<tr>
<td>Utility of post-Lyme disease failure state</td>
<td>0.6 (0.37-0.79)</td>
<td>42 900</td>
</tr>
</tbody>
</table>

*QALY indicates quality-adjusted life-year.

Table 5. League Table of Selected Cost Utility Analyses, With Ratios Converted to 1998 US Dollars

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Cost-effectiveness Ratio, $/QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hib vaccination vs no Hib vaccination in Australian children (aboriginal)</td>
<td>Cost-saving 70</td>
</tr>
<tr>
<td>Pneumococcal pneumonia vaccination vs no vaccination in worldwide birth cohort in 1988 in countries with very high, high, or middle mortality levels</td>
<td>4700</td>
</tr>
<tr>
<td>Selective HBV vaccination vs universal preadolescent HBV vaccination in population of country with low prevalence of HBV</td>
<td>18 000</td>
</tr>
<tr>
<td>Mammography screening vs no population-based screening in women 45-69 years old</td>
<td>36 000</td>
</tr>
<tr>
<td>Combination estrogen-progesterone therapy, 5 y of treatment vs no hormone replacement therapy in women at menopause averaging 50 years old</td>
<td>62 300</td>
</tr>
<tr>
<td>Vaccination against Lyme disease vs no vaccination of residents living in an endemic area</td>
<td>140 000</td>
</tr>
<tr>
<td>Diphtheria and tetanus toxoids with acellular pertussis vaccination vs existing DTP vaccination in worldwide birth cohort in 1988 in countries with very high, high, or middle &lt;5 mortality levels</td>
<td>590 000</td>
</tr>
<tr>
<td>Preoperative autologous donation of 2 U vs no preoperative autologous donation in patients undergoing primary, elective coronary artery bypass graft surgery</td>
<td>590 000</td>
</tr>
</tbody>
</table>

*Data are from Stone et al.\(^3\) QALY indicates quality-adjusted life-year; Hib, Haemophilus influenzae type b; HBV, hepatitis B virus; <5 mortality, mortality in children younger than 5 years; and DTP, diphtheria and tetanus toxoids plus pertussis vaccine.

In a recent cost-effectiveness analysis, Meltzer et al.\(^2\) examined the Lyme disease vaccination in terms of cost per case averted. There were a number of differences between the two studies including Meltzer and coworkers'\(^2\) inclusion of indirect costs in the base-case analysis, higher treatment costs, and assumptions that included higher probabilities of dissemination, for example. Our cost per case averted was $5300 for a seasonal attack rate of 0.01, which was not too different from Meltzer and coworkers. Our results in terms of QALYs allow comparison with other preventive interventions. For example, incorporating costs due to loss of work decreased the cost-effectiveness ratio of vaccination by about $10000/QALY saved. In addition, the model does not incorporate the cost of imperfect diagnostic capabilities of the clinician and laboratory tests or address the general fear and anxiety that residents of an endemic area experience as a result of their risk for Lyme disease.

Vaccination against Lyme disease does not protect against other tick-borne illnesses such as babesiosis and ehrlichiosis.\(^3\) Although the seasonal risk of these other tick-borne illnesses is currently less than that for Lyme disease, vaccination may increase the incidence of these illnesses since individuals may be less likely to take precautions. The use of precautionary behavior is an important aspect in determining the cost-effectiveness of a Lyme disease vaccine. For the purposes of this analysis, the attack rate estimates the current level of precautions taken by individuals in varying areas. If precautionary behavior were to increase, this would be reflected in the yearly attack rate (Figure 4). The cost of an intervention to change tick bite precautionary behavior is unknown at this time.
Lyme disease vaccination is approved for a 3-injec-
tion series over a 1-year period. Data suggest that an ac-
celerated vaccination series during a 6-month and 2-month
series may also be effective. This accelerated vaccina-
tion series increased the cost-effectiveness of the vaccina-
tion since there is a smaller likelihood that there will be
an episode of Lyme disease between the second and third
shot series if one assumes that full (2-year) efficacy shown
in the trials can be achieved in the first year.

Little is known about the duration of protection
against Lyme disease with the vaccination. We assumed
in this model that there would be adequate protection
for 1 year after the series is completed. In a sensitivity
analysis, the cost-effectiveness increased to $72,700/
QALY if a yearly booster shot is required for persisting
efficacy. One study shows that individuals vary in their
ability to mount an immune response against the OspA
protein, particularly with regard to age. It is likely that
both the duration and strength of protection against B
burgdorferi varies on an individual basis and additional
information is necessary to determine the true duration
of protection.

The availability of the Lyme disease vaccination is
an important adjunct in managing the increasing risk of
Lyme disease in endemic areas. Guidelines are neces-
sary for appropriate use of vaccination, both from an
individual and societal point of view. Our analysis, which
incorporates health state utilities and factors in manage-
ment costs of the late sequelae of Lyme disease, demon-
strated that in areas with a seasonal rate of Lyme disease
of greater than 1%, vaccination of individuals compares
somewhat favorably with other preventive treatments.
Resident living in these areas may be appropriate re-
cipients for vaccination against Lyme disease.

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