Clinical and Economic Impact of Improved Diagnostic Testing for Lyme disease

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Introduction

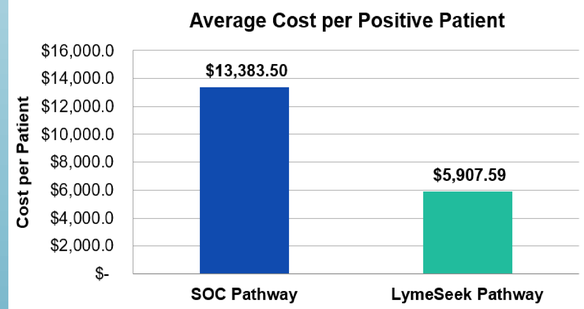
Lyme disease is a diagnostically challenging and under-reported infectious disease caused by the spirochete *Borrelia burgdorferi*. Delayed diagnosis, including misdiagnosis (reported by 72% of patients in a large U.S. patient registry), contributes to progression from localized and disseminated LD to Lyme-infection associated chronic illness (Lyme-IACI), which is associated with increased treatment costs and greater healthcare resource utilization (HCRU) through use of high-cost specialists. While claims-based studies estimate LD–related healthcare costs of up to $1.05 billion annually, current evidence is often limited to high-incidence regions of the U.S., and does not include the untracked costs incurred after a patient receives a misdiagnosis. Our objective was to develop an economic model to assess the true cost of LD in the U.S., and simulate how adoption of a more accurate diagnostic test that identified patients earlier in the infection impacted clinical and economic outcomes.

Method

A budget impact model (BIM) was developed by an independent health economics and outcomes research (HEOR) group to compare the current standard-of-care (SoC) diagnostic pathway with a pathway in which a novel higher-sensitivity diagnostic test is used. The model simulated an annual, national U.S. patient cohort for each scenario, tracking expected incidence of true- and false-positive and negative cases and quantifying subsequent progression to localized, disseminated, and Lyme-IACI. Stage-specific treatment costs were applied, and additional HCRU costs associated with false-negative (misdiagnosed) cases were incorporated. Model inputs, including clinical parameters, epidemiology, and healthcare costs, were derived from published literature and publicly available data sources, with all costs adjusted to 2025 U.S. dollars. Model structure and assumptions were validated through structured consultation with three major U.S. insurers.

Budget Impact Model – Patient Costs

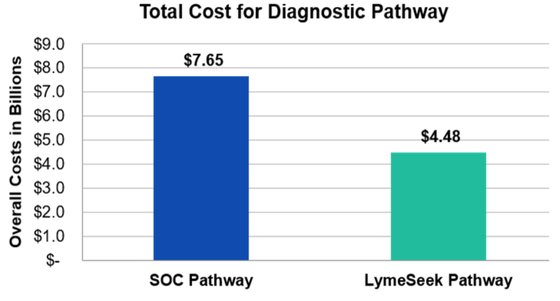
Use of LymeSeek, a test with high sensitivity and specificity in the first few weeks of *Borrelia* infection, increased early identification and treatment of LD patients during early stage infection, and substantially reduced false-negative test results.



Adoption of LymeSeek results in a 55.9% cost reduction per patient.

Budget Impact Model – Overall Healthcare Costs

Healthcare costs attributed to false-negative test results declined from $6.05 billion to $1.24 billion annually (79.53% reduction), largely driven by reductions in misdiagnosis-related HCRU ($3.75 billion vs. $0.76 billion).

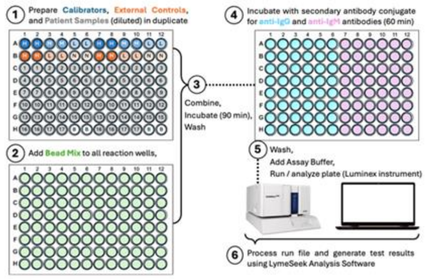


Adoption of LymSeek results in a 41.5% reduction in overall annual healthcare costs.

Multiplex flow immunoassay plus AI-derived algorithm

The LymeSeek Test:

LymeSeek is a multiplex flow immunoassay that uses color-coded microscopic beads to detect and quantify IgM and IgG antibody responses to eight *Borrelia* antigens in a single, small-volume sample. The LymeSeek algorithm was developed using a decision tree based machine learning model.



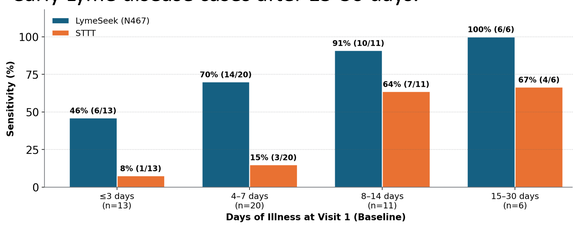
Summary of Results from BIM:

Clinical Outcomes (Patient, N)	SOC Pathway	Novel Diagnostic Pathway	Net Change (N, ±%)
Patients with True Positive Results (N)	**306,735**	**500,500**	**+193,765 (+63.17%)**
Patients with False Negative Results (N)	**243,265**	**49,500**	**-193,765 (-79.65%)**
Patients diagnosed with localized LD (N)	116,347	238,583	+122,236 (+105.06%)
Patients diagnosed with disseminated LD (N)	433,653	311,417	-122,236 (-28.19%)
Patients with post-treatment LD (N)	222,750	190,968	-31,782 (-14.27%)

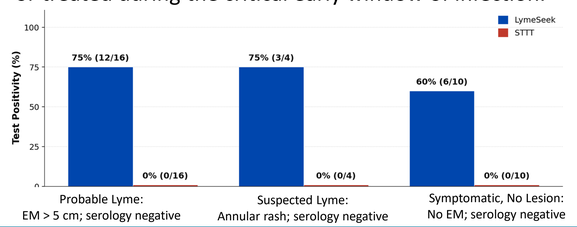
Economic Outcomes (US, $)	SOC Pathway	Novel Diagnostic Pathway	Net Change (US$, ±%)
Total Costs of LD Treatment ($)	**$3.57B**	**$2.36B**	**-$1.21B (-33.86%)**
Total costs of localized LD treatment ($)	$0.16B	$0.33B	+$0.17B (+105.06%)
Total costs of disseminated LD treatment ($)	$2.12B	$0.92B	-$1.19B (-56.35%)
Total costs of post-treatment LD ($)	$1.29B	$1.11B	-$0.18B (-14.27%)
Total Costs of Misdiagnosis ($)	**$6.05B**	**$1.24B**	**-$4.81B (-79.53%)**
Total additional HCRU costs due to misdiagnosis ($)	$3.75B	$0.76B	-$2.99B (-79.65%)
Total treatment costs of FN patients ($)	$2.30B	$0.47B	-$1.82B (-79.34%)
Total Costs for the Population ($)	**$7.65B**	**$4.48B**	**-$3.17B (-41.50%)**
Average Cost per Positive Patient ($)	**$13,383.50**	**$5,907.59**	**-$7,475.91 (-55.86%)**

Test performance in the diagnostic gray zone of early Lyme disease

JUH SLICE study (1): The test correctly identified nearly 50% of cases < 3 days of onset, and detected 100% of early Lyme disease cases after 15-30 days.



LDB (2): Samples from cases clinically diagnosed with Lyme disease, but serologically negative by a current standard of care diagnostic test compared to LymeSeek. These cases are representative of Lyme disease patients with false negative lab tests who would not be diagnosed or treated during the critical early window of infection.



Conclusions

- This BIM provides insights into potential savings in misdiagnosis-related healthcare costs, which are not well quantified in the existing literature.
- The increase in costs associated with mis-diagnosis leading to disseminated LD and Lyme-IACI are largely invisible to major U.S. insurers.
- By reducing misdiagnoses and increasing diagnosis of LD at an early stage, use of LymeSeek would improve clinical outcomes for Lyme disease patients.
- Patient clinical improvements are associated with meaningful economic savings through lower treatment costs and decreased HCRU.

References

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(2) Horn EJ, et.al 2026. Evaluation of standard and modified two-tiered testing algorithms using well-characterized early Lyme disease samples. J Clin Microbiol 64:e01187-25.