LYME DISEASE FIRST-LINE TREATMENT AND PROGRESSION IN FLORIDA AND THE NORTHEASTERN US: A COMPARISON USING REAL WORLD DATA

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BACKGROUND

Lyme disease, also *Lyme borreliosis*, is the most common tick-borne illness in the United States.[1] According to the CDC, the number of reported cases of Lyme disease in the US has been steadily increasing year-over-year in the last 25 years, having more than tripled over that period (see Figure 1).

Significantly, the geographic distribution of Lyme disease throughout the US has also increased, with the illness spreading to new areas in recent years, including the Southeastern US.[2] Outside the Northeastern US, Quest Diagnostics saw the largest absolute increase in positive Lyme disease test results between 2015 and 2017 in Florida and California, states where Lyme disease was not previously common.[3]

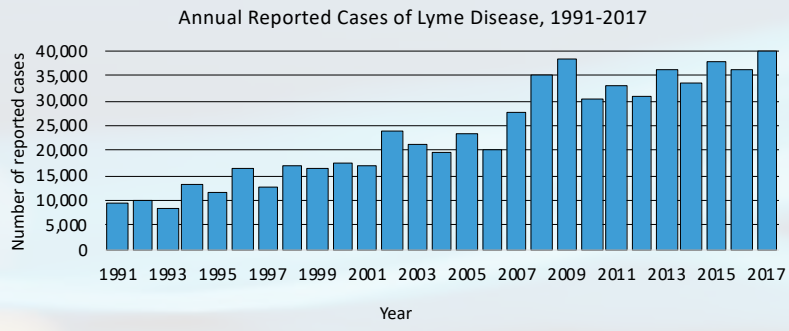

Figure 1: CDC data showing the number of Lyme disease cases reported to the CDC yearly from 1991 to 2017. A steady increase year-over-year is illustrated over the past 25 years. Source: literature[1]

OBJECTIVES

This study aimed to assess the implementation of IDSA- and EUCALB-recommended first-line treatment of early Lyme disease (ELD) and progression to later-stage Lyme disease (LSLD) in the Northeastern United States (NE) compared to Florida, utilizing a large real-world dataset:

- Do real-world data demonstrate decreased LSLD symptoms following recommended first-line treatment of Lyme disease?
- Does the percent of ELD patients who received recommended first-line treatment differ in the NE compared to Florida?
- Is there an increased risk of being diagnosed with LSLD in Florida, a state that has only recently seen large absolute increases in Lyme disease diagnoses, as compared to the NE?

METHODS

Data Source: The TriNetX platform was used to query a large electronic medical record (EMR) and payer dataset, providing access to aggregate counts on linked EMRs, pharmacy claims, and medical claims from approximately 190 million patients, with the majority of fact coverage from 2014 to 2018 (as of January 2019). The dataset contained 352,013 patients with a Lyme disease diagnosis.

Patient Cohorts: (see Figure 2) All patients were required to have a diagnosis of Lyme disease and at least 1 clinical fact (diagnosis, medication, or procedure) within 3 months to 1 year prior to, as well as within 3 months to 1 year following, their first diagnosis of Lyme disease. LSLD was defined as having at least one symptom commonly attributed to LSLD within 1 year of the first Lyme disease diagnosis. ELD patients, in contrast, could not have had such symptoms within the same time frame. To compare LSDL outcomes among patients treated with recommended first-line therapy and untreated patients, an additional cohort that had not had LSLD symptoms within 3 months after and anytime prior to their first Lyme disease diagnosis was identified. The treated cohort was required to have a recording of amoxicillin, doxycycline, or cefuroxime within 3 months of the first Lyme disease diagnosis, while the untreated cohort could not have had any of these medications within the same timeframe.

Outcomes Analysis: The proportion of patients with LSLD symptoms following treated and untreated Lyme disease was compared in a balanced outcomes analysis. Treated and untreated cohorts were matched on 20 covariates including age, sex, and baseline diagnoses via a 1:1 greedy-nearest-neighbor propensity score model. An outcome was defined as having at least one LSLD symptom within 3 months to 1 year following the Lyme disease index event. Risk and Kaplan-Meier (KM) patients were censored following the last fact in their record. Analyses were run to compare the outcomes associated with each cohort.

Zip Codes: Three-digit zip code data for patients' place of residence was used to determine which state they lived in. Patients from Florida or states in the Northeastern United States were included in the following analysis.

Regional Risk Analysis: Two risk analyses were conducted between patients with Lyme Disease in the Northeast and in Florida. The first analysis compared the percent of ELD patients who were treated with the recommended first-line therapy in the NE and Florida. The second evaluated the risk of Lyme disease patients being diagnosed with LSLD in each region.

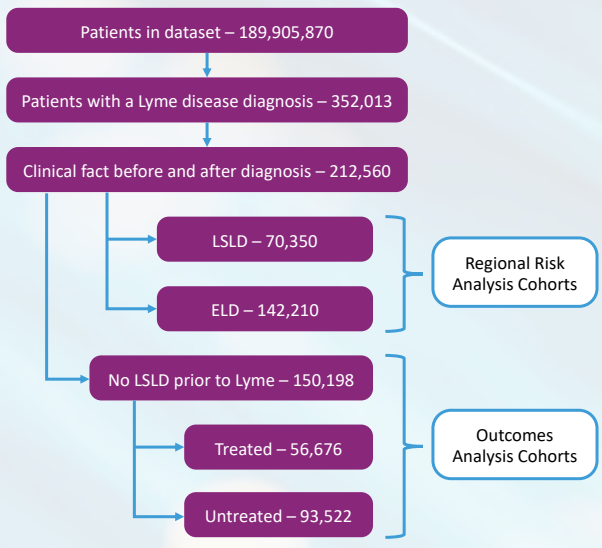

Figure 2: *Study populations and patient counts*

RESULTS

Outcomes Analysis:

- 93,522 and 56,676 patients were identified for the untreated and treated cohorts respectively, reduced to 54,289 patients each following 1:1 matching (Figure 3).
- A standard difference of >10% was observed in 9 covariates, reduced to 0 covariates following matching.
- The risk of developing LSLD was significantly lower in patients that received recommended treatment (5.1%) compared to patients that did not (6.5%). A censored KM analysis revealed a significantly lower survival probability without developing LSLD in untreated patients (92.7% vs. 94.4%) (all p<0.0001) (Figure 3).

Regional Risk Analysis:

- 135,835 patients with Lyme disease were identified across Florida and the NE. Of these, 92,542 experienced ELD symptoms and 43,293 were LSLD patients.
- Of ELD patients, a significantly lower proportion of patients received recommended treatment in Florida (21.8%) than in the NE (42.2%) (p<0.0001) (Figure 4).
- Additionally, a significantly higher proportion of total Lyme disease patients in Florida were diagnosed with LSLD (46.2%) than of Lyme disease patients in the NE (30.9%) (p<0.0001) (Figure 4).

It is important to consider that data coverage may differ by region. However, the alternate increased risks in both Florida and the NE indicate that coverage is fairly similar.

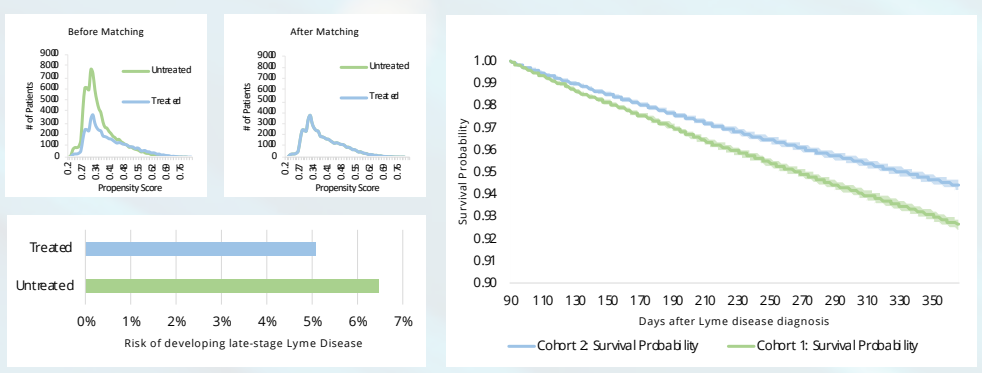

Figure 3: Top Left: *Propensity score distribution before and after matching; Bottom Left: Risk of developing LSLD in matched Treated and Untreated cohorts*; Right: *Kaplan-Meier Survival Analysis with 95% confidence bands*

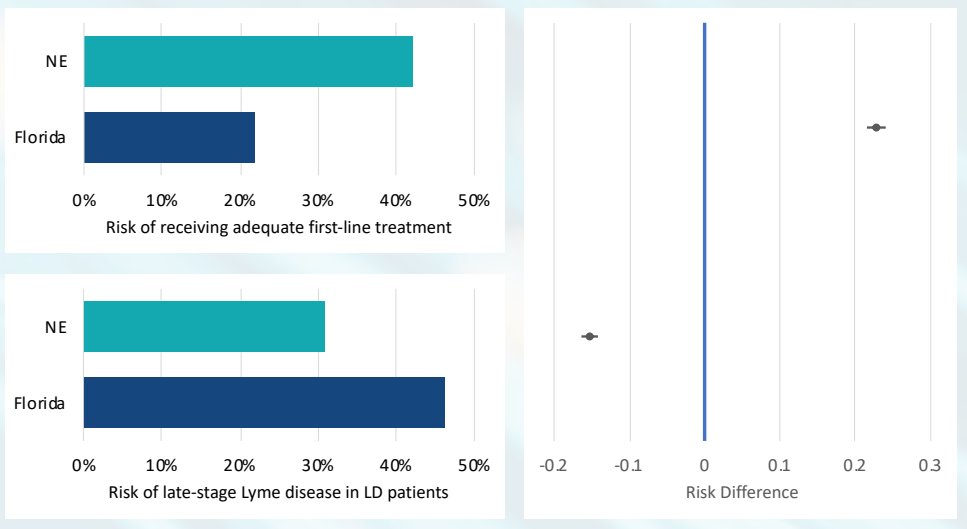

Figure 4: Top Left: *Proportion Lyme disease patients who received recommended first-line treatment in the NE and Florida;* Bottom Left: *Proportion of Lyme disease patients with LSLD in the NE and Florida;* Right: *Respective risk differences (with CI) between the NE and Florida*

CONCLUSIONS

- Lyme disease patients who have been treated with IDSA- and EUCALB-recommended first-line treatment of ELD show significantly fewer LSLD symptoms within 3 months to 1 year following their first Lyme disease diagnosis.
- While it is known that Lyme disease is rapidly on the rise in Florida, these data indicate a significant deficit in the administration of recommended first-line treatment of Lyme disease in Florida.
- We also find a much higher proportion of patients to have developed LSLD in Florida as compared to in the Northeastern US.
- These results signify that increased training/communication efforts may be warranted for Florida physicians to diagnose Lyme disease patients early in their disease and follow recommended first-line treatment.

(1) *Why Is CDC Concerned about Lyme Disease? | Lyme Disease | CDC*. 20 Dec. 2018, https://www.cdc.gov/lyme/why-is-cdc-concerned-about-lyme-disease.html.
(2) Stone, Brandee L., et al. "Brave New Worlds: The Expanding Universe of Lyme Disease." *Vector Borne and Zoonotic Diseases*, vol. 17, no. 9, Sept. 2017, pp. 619–29. *PubMed Central*, doi:10.1089/vbz.2017.2127.
(3) *Health Trends: Lyme Disease*. Quest Diagnostics, July 2018, https://questdiagnostics.com/dms/Documents/health-trends/Quest_LymeDiseaseTrendsReport_2018.pdf.