



MyLymeData

PROJECT OF LYMEDISEASE.ORG



2019 Chart Book | MyLymeData Registry

MyLymeData expects to gather more data about Lyme disease than any other research study has done before.



Source Of Data

The data in this report was collected during Phase 1 of MyLymeData and consists of self-reported data for 3,903 US patients diagnosed by a healthcare provider with Lyme disease. MyLymeData is a fully consented patient registry that has been approved by Advarra Institutional Review Board.

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Additional Resources

This report can be downloaded at <https://www.lymedisease.org/mylymedata-lyme-disease-research-report/>

To enroll in MyLymeData, visit www.MyLymeData.org.

For more information about findings from the registry, visit the MyLymeData Viz Blog at <https://www.lymedisease.org/mylymedata-viz-blog/>.

Conflicts of Interest

The authors declare no conflicts of interest.

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We thank the patients participating in MyLymeData, who have the power to accelerate research in Lyme disease and without whom this research could not have been done.

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About LymeDisease.org

Founded 1989

LymeDisease.org is one of the oldest Lyme disease 501(c)(3) nonprofit organizations in the nation. For over 30 years we have worked to make the patient voice stronger, to support patient-centered research, to promote legislative change, and to create a future where Lyme patients can receive the treatments they need to get well. We do this through patient empowerment and science-based advocacy—a powerful combination.

Empowering Patients

We strive for patient involvement at all levels of decision-making, from research project selection, guideline development, and individualized treatment decisions. We advocate for patient voices to be heard in health policy-making and at the physician's office.



We Believe:

Lyme patients must have access to quality medical care.

Patient care should be patient-centered and address the needs of patients.

Patients are entitled to make choices about their treatment options.

Physicians must give patients the information they need to make informed choices.

Research that matters to patients must be funded.

Patient-driven research that is clinically relevant is necessary for progress.

***“Start where you are. Use what you have.
Do what you can.”***

-Arthur Ashe



Lyme disease community, friends and supporters

We are pleased to present the highlights of the MyLymeData patient registry data. Since MyLymeData was launched in November 2015, it has enrolled over 12,000 participants and is currently among the top 5% of fully consented, opt-in patient registries in the nation. The registry captures a broad range of data on the health of those living with Lyme disease and uses this information to help advance our understanding of the disease, how it progresses, and the effectiveness of treatment interventions. The ultimate goal of MyLymeData is to improve healthcare for all people with Lyme disease.

We are excited that our first study analyzing registry data was recently published in the peer-reviewed, open access journal *Healthcare*. We are also delighted to be collaborating on a tissue collection project with the National Disease Research Interchange, the leading source for research tissues in the nation, and the Bay Area Lyme Foundation Tissue Bank. In addition, we have collaborated with academic researchers at the University of California at Los Angeles and at the University of Washington. The National Science Foundation has funded UCLA researchers to explore big data analytics using data from our registry. These are essential steps in building a collaborative research engine designed to realize the promise of big data and accelerate research in Lyme disease.

This report highlights our progress since launch and reviews select descriptive data from Phase 1 of the project, which ran from November 2015-2016. It reflects the efforts of the registry team and the vital contributions of patients in making the registry a success.

We hope you find this report informative and that it sparks discussions about the value of this type of data for the Lyme disease community. We believe that this is a truly exciting time in Lyme disease for research with advances being made in diagnostic testing, big data, and the promise of precision medicine.

We are deeply grateful to everyone who has supported this work—particularly the patients with Lyme disease who make this work possible by generously sharing their information.

A handwritten signature in blue ink, appearing to read 'L. Johnson'.

Lorraine Johnson, JD, MBA
CEO of LymeDisease.org
Principle Investigator of MyLymeData

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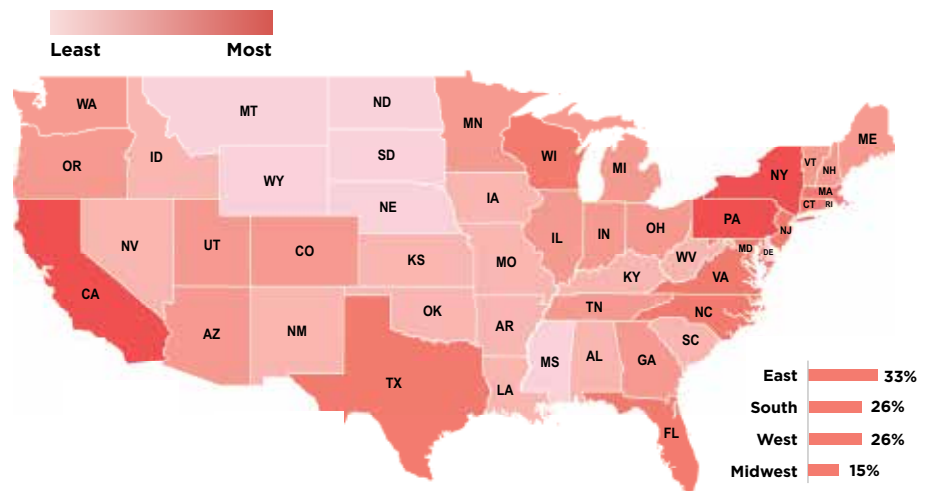
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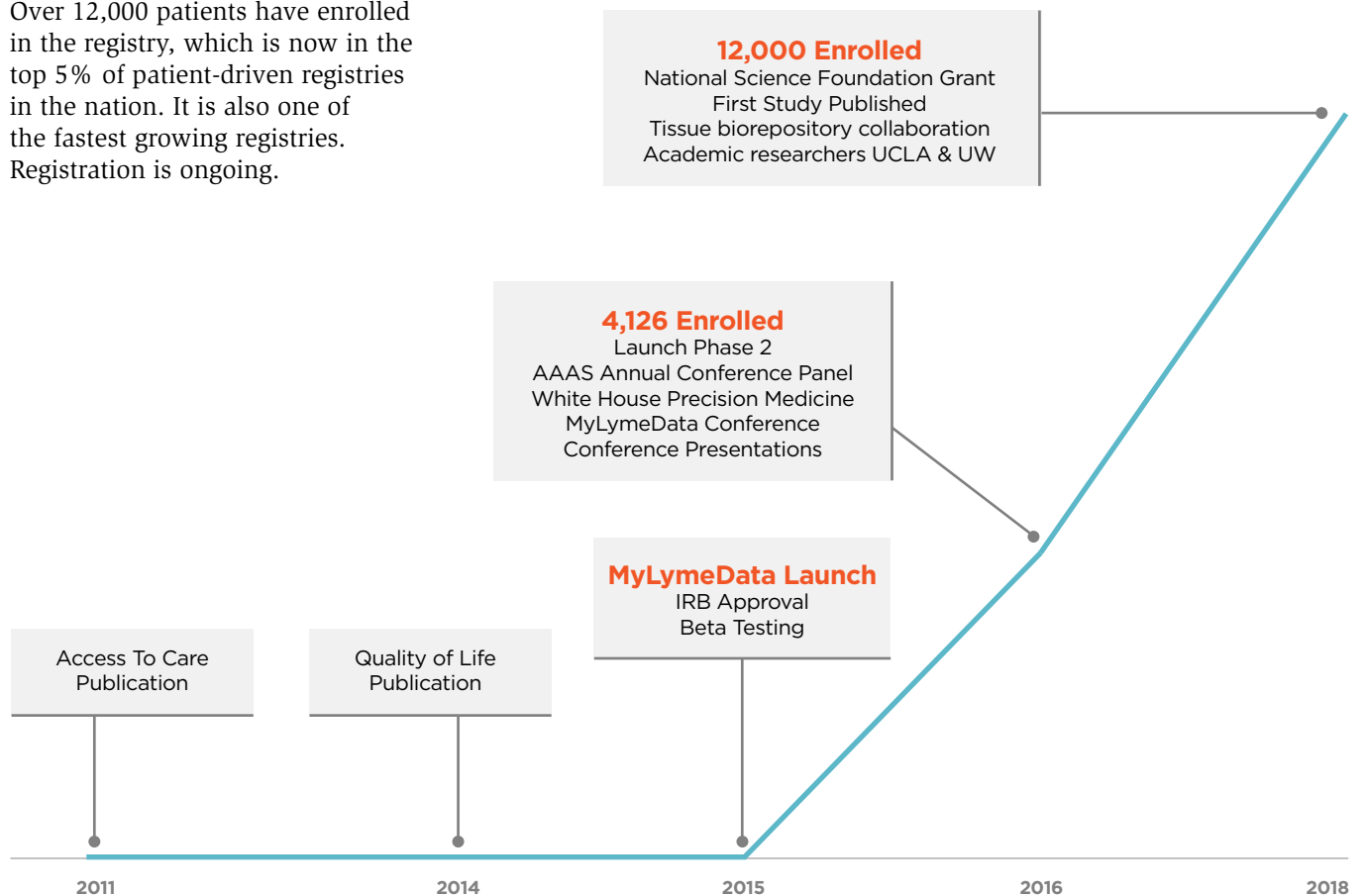
MyLymeData

MyLymeData is a patient registry and research platform that was developed and launched by LymeDisease.org in 2015. It uses big data research tools that allow patients to quickly and privately pool their data to determine which treatments work best. The registry includes patients enrolled from every state. This map reflects patients enrolled in the registry from November 2015 to November 2017.



One Of The Fastest Growing Registries

Over 12,000 patients have enrolled in the registry, which is now in the top 5% of patient-driven registries in the nation. It is also one of the fastest growing registries. Registration is ongoing.



Highlights of MyLymeData Patient Registry

Analysis of Phase 1 Data (November 2015-2016)

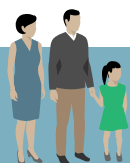
Lyme disease is caused by the spirochete *Borrelia burgdorferi* and is transmitted primarily by tick bite. It is the most common vector-borne disease in the United States.

The Centers for Disease Control and Prevention (CDC) estimates that 300,000 cases of Lyme disease occur annually. Patients diagnosed and treated early generally respond well to treatment. However, treatment failures ranging from 10-35% have been reported in early disease and higher rates are reported for late disease.

Very little research has been conducted regarding how best to treat patients who do not respond to short-term

treatment approaches or who are not diagnosed early. MyLymeData was developed to accelerate research in Lyme disease by providing observational data and serving as a research platform for more traditional studies. Most of the patients in MyLymeData (79%) identify their current stage of illness as late (16%) or chronic Lyme disease (61%).

The majority of patients in the registry report were diagnosed late (70%), when treatment success is much more difficult to achieve. **Fewer than 13% of patients in the registry were diagnosed within the critical first month.**



12,000+
enrolled to date

51%
>3 years to
diagnosis

78%
of diagnosis
supported
by serology

72%
misdiagnosed
before Lyme
diagnosis

89%
willing to
participate in
research

60%
diagnosed
with
co-infection

70%
not diagnosed
until late stage
(> 6 months)

53%
saw ≥5
clinicians

BIG DATA RESEARCH

Data-Driven Healthcare Policy

For over 10 years, LymeDisease.org has played an instrumental role in science-based advocacy nationally and internationally, participating in leadership roles for government-sponsored patient-centered healthcare, evidence-based medicine, big data efforts, and Lyme disease public policy initiatives. It has also published in peer-reviewed publications on these topics.

Members of LymeDisease.org have participated, served on panels, and presented before national healthcare policy organizations including:

- The Patient Centered Outcomes Research Institute (PCORI) (Advisory Panel)
- PCORnet (PCORI's big data project) (Executive and Steering Committees)
- PCORI's Open Data Expert Panel
- Cochrane Collaboration
- Consumers United for Evidence-Based Healthcare (Steering Committee)
- The National Institute of Health Collaboratory (NIH's big data project)
- The Institute of Medicine Convening: Working Towards High Value Care
- The White House Precision Medicine Initiative
- Health and Human Services (HHS) Tick-Borne Disease Working Group Subcommittees

- Society to Improve Diagnosis in Medicine (Patient Partner)
- American Institutes for Research Center on Knowledge Translation
- The HHS Lyme Innovation Initiative
- Stanford MedX

The central thrust of many of these initiatives recognizes that the traditional clinical trial research model is inefficient. These efforts seek to accelerate the pace of research, to make it more patient-centered, and to develop a learning system of healthcare where research findings are informed by and implemented into real world clinical practice. There is a clear need to adopt this approach in Lyme disease research, where clinical trials move at a glacial speed and exclude most patients seen in clinical practice.

The few clinical trials in Lyme disease that the NIH has funded utilized very small samples (ranging from 37 to 129), took 2.5 to 5 years to complete recruitment alone, and screened out between 89% and 99% of those who applied, resulting in study samples that were not representative of the overall population of chronic Lyme disease patients. In contrast, one of our big data surveys recruited over 3,000 patients in six months. With big data, we can and must accelerate the pace of clinical research and include real world patients.

Lyme Disease Study Comparison

Screened | Enrolled | Years



BIG DATA RESEARCH

Why Does BIG DATA Matter?

MyLymeData is research done differently. It is the first national large-scale study of chronic Lyme disease. This study is different from all other Lyme disease studies because it's patient-powered BIG DATA research.

TO SOLVE BIG PROBLEMS YOU NEED BIG DATA



All of the previous treatment trials for chronic Lyme disease were very small—ranging from 37 to 129 participants. Compare that to MyLymeData—which has enrolled over 12,000 patients. The problem with small trials is they don't give you much information.

Big data studies provide lots of information so that we can look at whether some groups of patients respond better than others to treatment..

BIG DATA LOOKS AT TYPICAL PATIENTS



Traditional NIH studies of chronic Lyme disease screened patients using highly restrictive criteria that excluded most typical patients. Because of this, those in the study may not be like those seen every day in clinical practice. This means the results of the study may not apply to typical patients.

Big data uses very broad entry criteria. Anyone in the United States who has been diagnosed with Lyme disease can enroll.

BIG DATA ALLOWS LONGER TERM STUDIES



Traditional treatment studies measure only one treatment intervention for a short period of time. For example, the NIH treatment studies used only one antibiotic at a time and the longest duration of treatment was 90 days.

Big data examines treatments used in the real world for durations that clinicians are actually using to see what works.

BIG DATA RESEARCH

Patient-Driven Research

The goal of MyLymeData is to:

- Foster research partnerships,
- Build the Lyme community research capacity,
- Develop a group of research-ready participants for clinical trials, and
- Accelerate the pace of research.

MyLymeData is part of the patient-centered research movement that seeks to transform the traditional research hierarchy in which studies are conducted on passive patients into a partnership model between patients and researchers. This approach is attractive because it advances co-creation of research, promotes patient-centered methods, and develops research capacity.

Patients are the most underutilized resource in medicine. As the central participants in the healthcare process, patients can draw upon many sources of personal health data that are locked in separate electronic health records, insurance records, clinician notes, or research silos. Data

collected from patients may be more complete than data from other sources.

Patient-generated data is unique in that patients, rather than providers, capture and record the data. The CDC, the NIH, the Food and Drug Administration (FDA), and PCORI each have launched registries that rely on patient-generated data. FasterCures, a non-profit that focuses on accelerating medical research, reports that over 110 such registries have been launched.

Unlike traditional trials, patient registries are uniquely suited to:

- Enroll diverse patient populations,
- Evaluate care as it is actually provided in real-world practice,
- Assess complex treatment patterns and treatment combinations, and
- Evaluate patient outcomes when clinical trials are not practical or are difficult to conduct (for example, when long-term outcomes are important).

As the graph below illustrates, patient registries play a vital role by linking with biorepositories, helping develop the disease knowledge base, shaping clinical trial hypothesis, speeding up recruitment times, expediting FDA approval and reducing the burden of post-approval studies. (Derived from Groft 2014)

Patient Registries Partner to Develop Intervention Pathways



BIG DATA RESEARCH

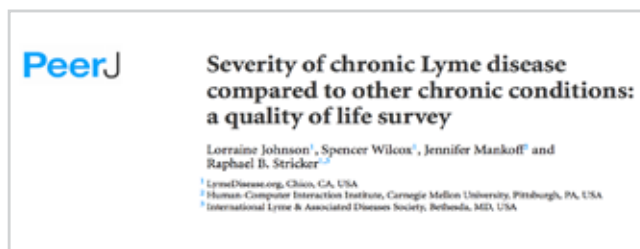
Big Data Surveys

LymeDisease.org began collecting patient-generated data over 10 years ago through surveys. We have published the results of two of these prior surveys—one focusing on access to care and the other on quality of life—in peer-reviewed journals. Unlike traditional clinical trials which have struggled with small sample sizes (149 was the largest), these surveys engage thousands of patients. (Johnson 2011, Johnson 2014). In 2018, we published the first study using data from the MyLymeData patient registry. (Johnson 2018)

These publications include previously unpublished information about patients with chronic Lyme disease (for example the percentage of patients who

also have one or more co-infections). Because of this, the open access publications in particular have received considerable attention. For example, our 2014 publication drew over 26,000 views, 6,000 downloads, and 21 citations. The 2018 study was published less than three months ago, and has already drawn over 5,000 views and 2,800 downloads.

This report will briefly review notable findings from the first two big data studies conducted by LymeDisease.org and then discuss some of the results from the analysis of data from the MyLymeData patient registry.



“[Recent trials] emphasize the role of engaging patients in... generating their own data. Patients have long been neglected for having a more active role in their care, when in fact, given the appropriate tools, they represent true 'blockbuster' potential for improving their outcomes.”

-Eric Topol, MD
Editor-in-Chief, Medscape

ACCESS TO CARE STUDY

Time to Diagnosis

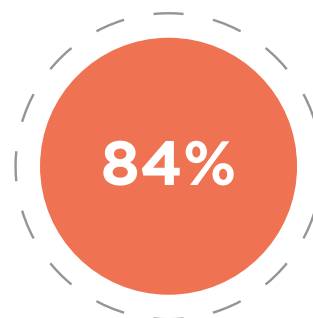
Our first published study focused on access to care, which can reduce the incidence of preventable diseases, provide early detection and diagnosis of treatable diseases, and reduce mortality and morbidity of chronic diseases. (Johnson, 2011) While early diagnosis and treatment are usually effective, when diagnosis is delayed treatments are much less effective and cure may be elusive. In Lyme disease, access to care is a significant issue.

Barriers to care may be geographic, financial, or systemic structural factors that result in failure to provide needed services. Key factors include insurance coverage, healthcare costs, travel time and distance to obtain care, and availability of care. Most patients with persistent disease see many doctors before diagnosis, are diagnosed late in the course of their disease, and travel significant distances to receive care.



Most patients **(95%)** are diagnosed by primary care clinicians.

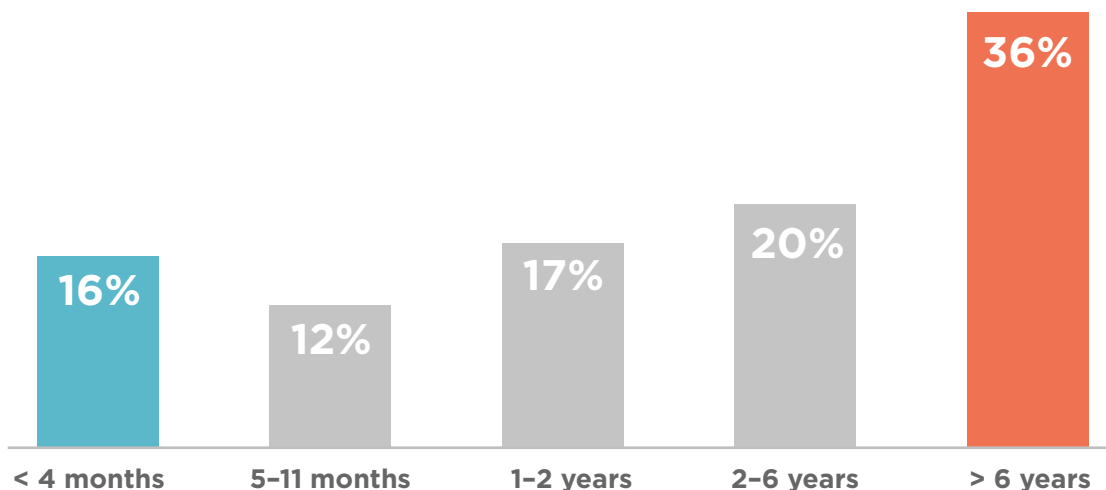
Only 5% of patients are diagnosed by infectious disease specialists.



How long before diagnosis?

36% of Lyme patients were unable to receive a diagnosis before **at least six years** of illness.

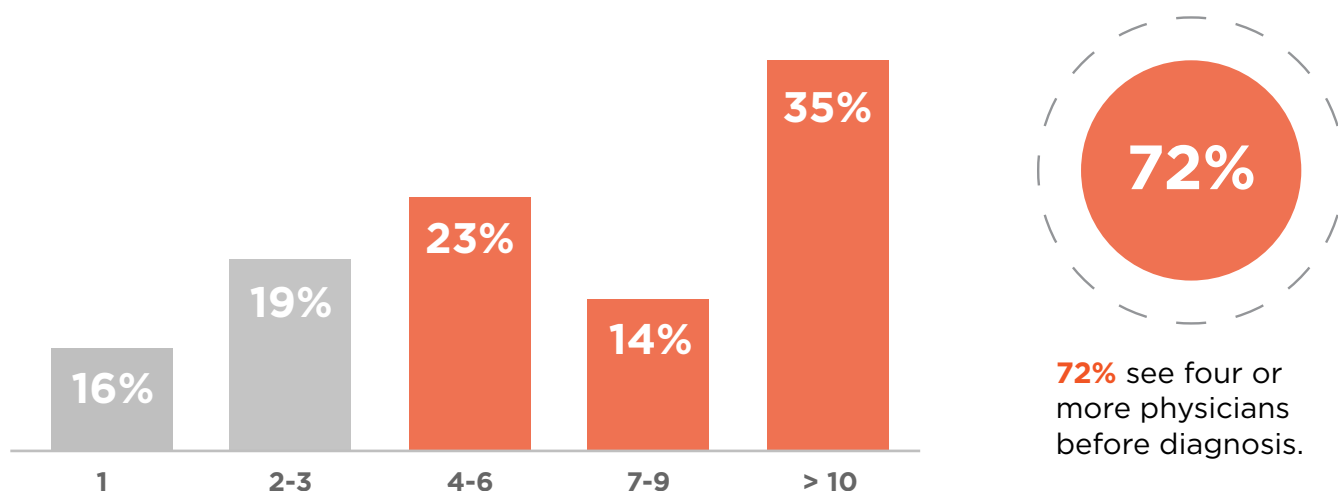
84% of Lyme patients were not diagnosed within the **first 4 months** of illness.



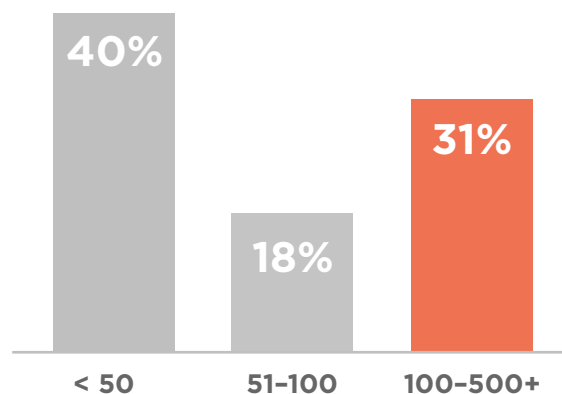
How Many, How Far?

Most patients see more than four physicians before they are diagnosed, creating delays that may profoundly impact their quality of life. To obtain care, 49% must travel more than 50 miles. The cost, inconvenience, and work-related impact of traveling these distances may result in many patients foregoing care all together.

How many physicians before diagnosis?



How many miles to treatment?



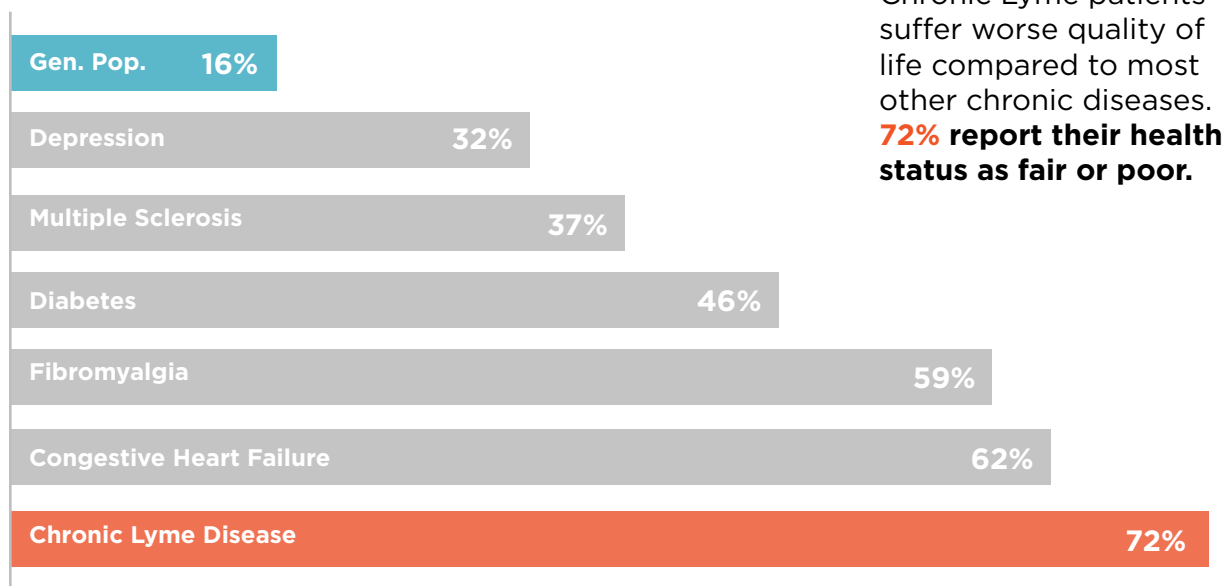
QUALITY OF LIFE STUDY

Poor Health Status

Another LymeDisease.org large-scale patient survey, “Severity of Chronic Lyme Disease Compared to Other Chronic Conditions: A Quality of Life Survey,” included over 3,000 patients and assessed health-related quality of life, burden of disease, and symptom severity. (Johnson 2014) To be included in the study, patients had to be diagnosed by a clinician and remain ill for at least six months after being treated with 10-21 days of antibiotics.

This study utilized standard survey questions developed by the CDC and the Agency for Healthcare Research to determine the burden of disease compared with different diseases. The survey showed that chronic Lyme disease patients have a quality of life that is significantly worse compared to the general population, and people with multiple sclerosis, diabetes, and congestive heart failure.

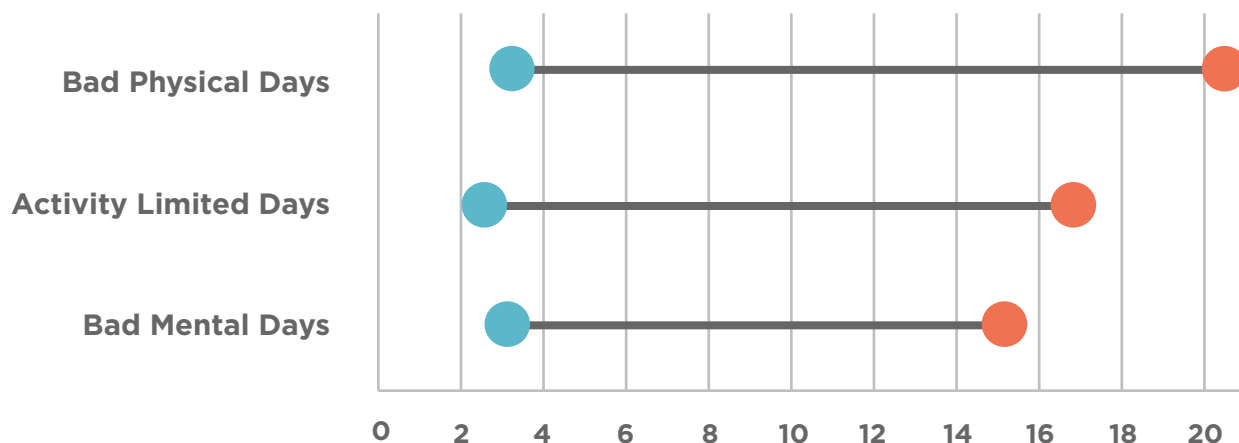
Health Status As Fair Or Poor



Chronic Lyme disease patients also have more bad physical, mental, and activity limited days in a month compared to the general population. Because of this, their quality of life is reduced, as is their ability to participate in work and family-related activities.

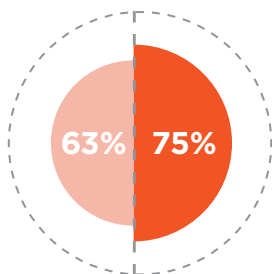
Chronic Lyme Patients Have More Bad Health Days Per Month

General Population vs. MyLymeData Patients



QUALITY OF LIFE STUDY

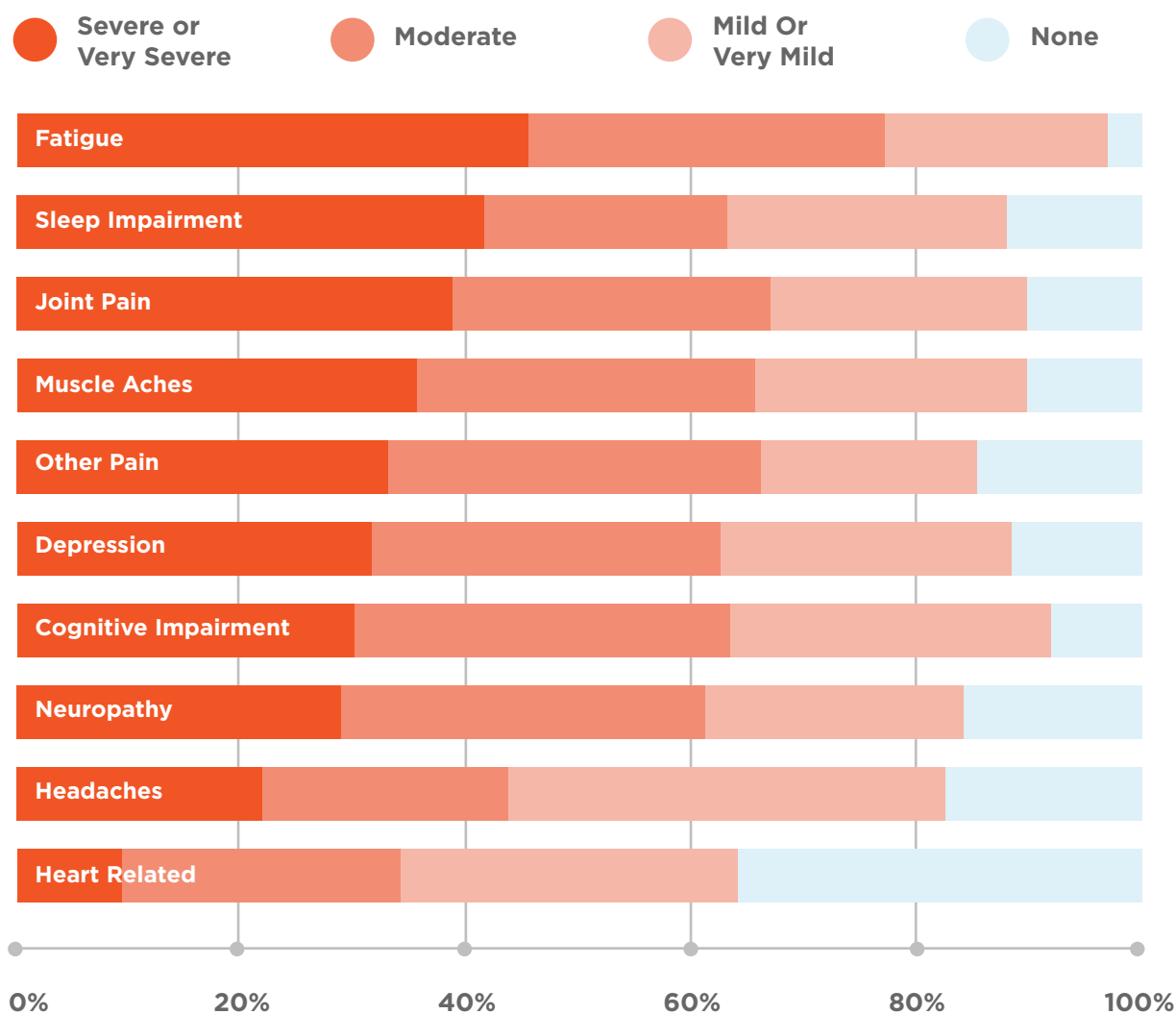
Symptom Severity



75% of Lyme patients experience severe or very severe symptoms.

63% describe two or more symptoms as severe or very severe.

In the quality of life study, patients with chronic Lyme disease also rated the severity of their symptoms. Previous studies on Lyme disease reported frequency of symptoms, but not symptom severity. (Johnson 2014) This chart shows the most commonly reported symptoms and how patients rank their severity. The severity of symptoms suffered by Lyme disease patients helps distinguish Lyme disease from the “aches and pains of daily living.”



MyLymeData Registry & Research Platform



MyLymeData is an expansion of our work in patient surveys. Phase 1 of the study was launched in November 2015. The National Science Foundation awarded an \$800,000 three-year grant to a UCLA research team headed by UCLA Mathematics Professor Deanna Needell to explore big data predictive analytics approaches using the MyLymeData registry.

Phase 1 of MyLymeData, which ran from November 2015 to November 2016, enrolled 4,719 patients. The data collection from Phase 1 is completed and is currently being analyzed.

To be included in the study, patients were required to reside in the US and to have been diagnosed with Lyme disease by a healthcare provider. After exclusions, the total sample size for Phase 1 was 3,903. Of these 3,556 reported still being ill, while 347 reported being well.

| Phase 1 Sample Determination and Characteristics | |
|--|-------|
| Enrolled | 4,719 |
| Exclusions | |
| Duplicates and incompletes | 113 |
| Non-US | 375 |
| Not diagnosed by healthcare provider | 328 |
| Final Sample Size | 3,903 |
| Unwell | 3,556 |
| Well | 347 |

The first study based on data from the registry, "Removing the Mask of Average Treatment Effects in Chronic Lyme Disease Research Using Big Data and Subgroup Analysis," was published in October 2018 (Johnson 2018).

Survey questions were drawn from standardized government survey banks, other widely used instruments (such as the 36-Item Short Form Health Survey [SF-36] developed by RAND or the Global Rating of Change Scale as well as peer-review published studies and past Lyme disease surveys, including two published studies conducted by LymeDisease.org (each enrolling over 2,400 patients).

LDo developed additional survey questions regarding severity of symptoms, treatment, and clinical presentation of Lyme disease. Face and content validity of novel survey questions were established through review by expert clinicians and patients. The questions were then beta tested by a subgroup of over 300 patients and revised accordingly.

All surveys also include a diagnosis validation question set that reflects questions commonly asked by healthcare providers when making a diagnosis. These questions permit researchers to select different inclusion criteria for any data set being analyzed. For example, a previous study included only respondents who (a) were clinician-diagnosed with Lyme disease, (b) had either an erythema migrans (EM rash) or positive serology, and (c) who remained ill for six or more months following treatment with antibiotics. This sample was then compared with another selection criteria set which included only those with EM rash or CDC two-tiered positive serology. (Johnson 2014)

Diagnosis validation questions:

- Diagnosis by a clinician
- Signs or symptoms
- Exposure
- Recall tick bite
- EM rash
- Positive lab tests
- Co-infections
- Functional impairment

Sources of questions:

- CDC-developed surveys, including Behavioral Risk Factor Surveillance System, National Health Interview Survey, National Ambulatory Medical Care Survey, and National Center for Health Statistics
- Rand SF-36
- Agency for Healthcare Research and Quality Medical Expenditure Panel Survey
- Past surveys and peer-review published literature

Sample and Diagnostic Characteristics

(Phase 1 sample size: 3,903)

Key Diagnostic Factors

| | |
|--------------------------------------|------|
| Clinician diagnosed (entry criteria) | 100% |
| Recall tick bite | 41% |
| Recall EM rash* | 34% |
| Supporting lab tests | 78% |
| ≥ 1 co-infection | 60% |



70% not diagnosed until **late stage**

Current Stage Of Illness

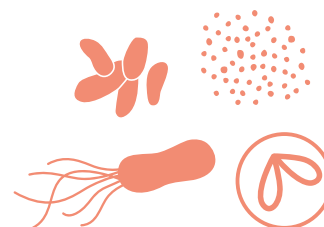
| | |
|--------------------------------|-----|
| Chronic LD [†] | 61% |
| Late Untreated LD [‡] | 18% |
| Early LD [§] | 6% |
| Don't Know / Other | 15% |



72% initially **misdiagnosed**

Demographics

| | |
|----------------------------------|------------|
| Female | 83% |
| Mean Age | 49 |
| <i>Education</i> | |
| High School or Less | 340 (9%) |
| Some College or Associate Degree | 1265 (34%) |
| Bachelor Degree | 1139 (31%) |
| Graduate School Degree | 945 (25%) |



60% diagnosed with one or more **co-infection(s)**

* Because of a branching error in the initial survey, patients were re-asked this question. This data includes the 1190 who responded to the revised question.

[†] Remained ill for ≥ 6 months after treatment with antibiotics for 10-21 days

[‡] Diagnosed ≥ 6 months after symptom onset

[§] Rash, flu-like illness, headache etc.

Identifying “Super Responders” is Key

The first study using information from MyLymeData has just been published in the medical journal *Healthcare* by Johnson, Mankoff, and Shapiro. (Johnson 2018) Using patient-reported outcome data from 3,903 people enrolled in MyLymeData, we looked at how individual patients vary in their response to treatment. Finding out who responds well to which treatments—and then learning more about those people—is an important step towards developing personalized Lyme disease treatment.

We know a lot about how to treat early Lyme disease, but even so treatment failure rates remain unacceptably high (10-35%). We know very little about what works—what is effective—for treating late or chronic Lyme disease. Researchers in other diseases such as tuberculosis, pulmonary disease, and cancer have tackled treatment variation challenges by identifying high treatment responders. Our study is the first to use this approach in Lyme disease. Randomized controlled trials in Lyme disease have been too small (37-129 people) to permit identification of subgroups of treatment responders.

As the figure illustrates, averages can overlook important details when there is treatment variation among individuals because the favorable response of one patient is canceled out by the negative response of another. (Derived from Kravitz 2004). A better approach looks at variations in how different patients respond.

Big data analytics are expected to play a critical role in the emergence of personalized medicine and

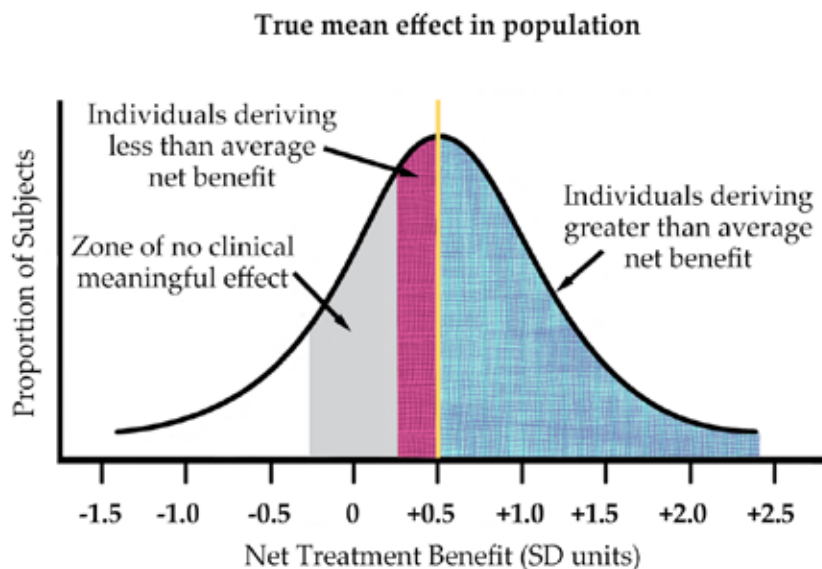
individualized care. To harness the full benefits of personalized healthcare will require more efficient research practices and big data analytics to discover deep knowledge about patient similarities, personalized disease risk profiles, and treatment response variation. Medical decisions are made for individuals, and assessment of the variation in treatment response is critical as medicine seeks to become more personalized and patient-centered.

Using a validated global rating of change scale question from other peer-reviewed studies, we asked patients to specify the level of their treatment response in detail. First, patients were asked if their condition was better, unchanged, or worse following antibiotic treatment:

Since antibiotic therapy, I would say my symptoms are...

- Better
- Unchanged
- Worse

If a respondent answered better, they were asked to rank how much better, on a scale of 1 to 7 (ranging from “hardly better at all” (1) to “a very great deal better” (7). Those who answered worse were given a similar follow-up question. Global rating of change scales can be used in all forms of research as a study end-point to assess treatment response. This simple two-step question approach is useful not only in patient registries, but also in randomized controlled trials and in pragmatic healthcare provider standard-of-care studies and may provide a common bridge between research approaches.



Treatment Response Variation in Lyme Disease

As the chart below details, more than half (52%) reported at least some improvement with antibiotic treatment and many (34%) stated that they improved “moderately” to “a very great deal.” Slightly more than a third (37%) had no treatment response. Only 12% reported that their symptoms were worse after treatment.

Patient response to treatment

Much better | Better | Same | Worse | Much worse



Looking only at “average” figures, there was little response to treatment (1.7). However, identifying how sub-groups of patients vary in their treatment response reveals an entirely different picture, making it clear that treatment response varies considerably among patients. This approach allows us to distinguish the 34% of patient who were high responders, reporting moderate to a very great deal of improvement in response to treatment. The treatment response of this subgroup was substantial—5.3 on a 7 point scale.

The 34% who report being significantly better are considered high treatment responders. As Dr. Allen Roses, former head of the pharmaceutical company GlaxoSmithKline, points out, understanding why these patients respond well to treatment could help us understand better treatment approaches for patients. As noted previously, randomized controlled trials of Lyme disease in the past have been too small to permit identification of subgroups of treatment responders.

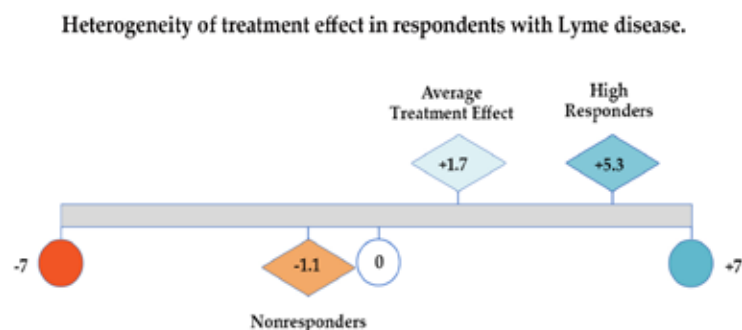


Figure 3. Average treatment effect, high responders and nonresponders on GROOC scale shows heterogeneous treatment response among participants that average treatment effect masks.

“The vast majority of drugs - more than 90 per cent - only work in 30 or 50 percent of the people. Drugs out there on the market work, but they don’t work in everybody. . . The idea is to identify ‘responders’ - people who benefit from the drug.”

-Dr. Allen Roses, Chief of GlaxoSmithKline (2002)

DIAGNOSIS

Early Symptoms

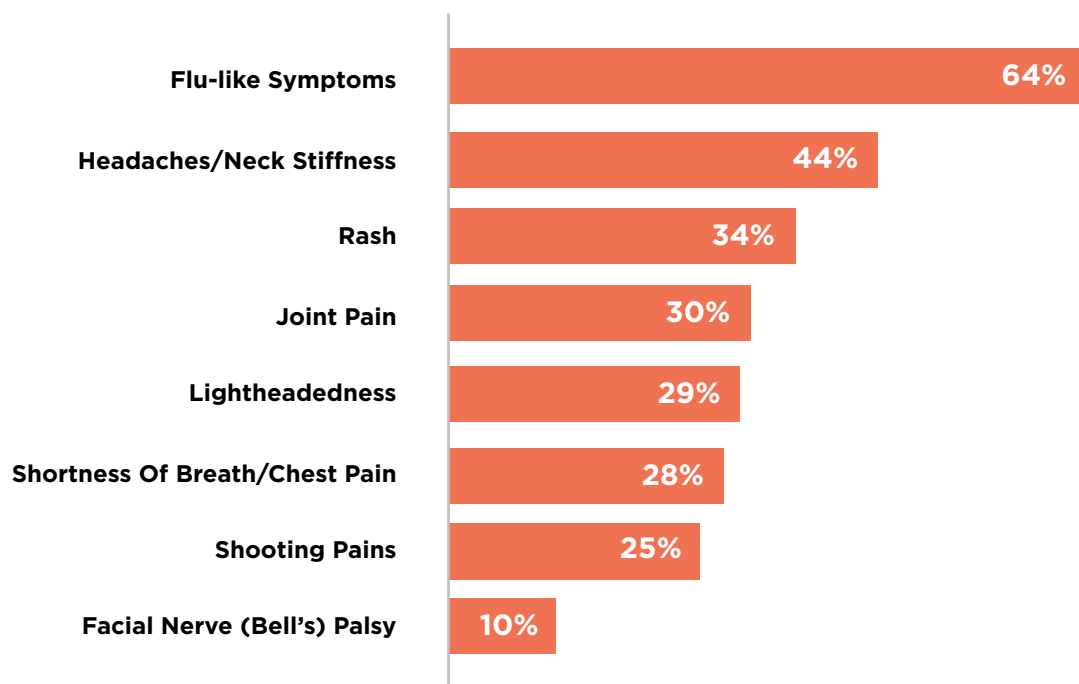
Only 34% of the patients in MyLymeData report a rash, but many more report non-specific flu-like symptoms (64%) or headache (44%).* This makes misdiagnosis more likely. Aucott reports that 54% of Lyme disease patients who present without a rash are misdiagnosed. Patients who are not diagnosed until late-stage Lyme disease (70% of this sample) may be less likely to have a rash or to have noticed a rash and this may have contributed to their delayed diagnosis.



More patients report early Lyme disease **flu-like or headache/stiff neck symptoms** than a rash.

Early Symptoms Of Lyme

“Within days to weeks after exposure, I developed...”



Rash rates vary in studies and surveillance criteria and may reflect differences in the populations studied. For example, more patients with a rash may be included in the CDC surveillance definition, which emphasizes the rash. Studies of early Lyme disease may also reflect a higher rash rate, particularly if this is an “objective” measured finding of the study.

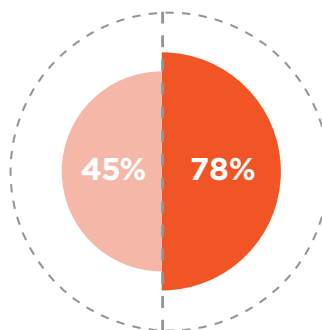
* Because of a branching error in the initial survey, patients were re-asked this question. This data includes the 1190 who responded to the revised question.

In addition, strain-specific variation of *Borrelia* may affect rash rates. CDC surveillance rash estimates vary widely depending on the state, ranging from 51% in Delaware to 87% in Minnesota. (Johnson 2014) Maine reports only 43% with a rash. (DHHS Maine 2014) Accordingly, considerable geographic variation appears to be a factor.

DIAGNOSIS

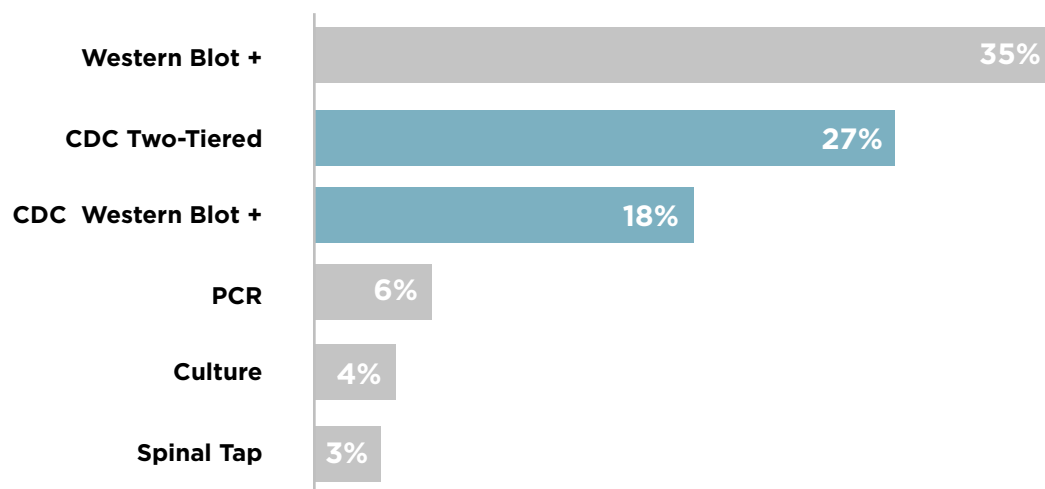
Lyme Disease and Co-infection Testing

The majority (78%) of patients in MyLymeData report that their diagnosis was supported by positive lab tests, and 45% of these reported that their tests were positive by either two-tiered testing or a stand alone western blot based on CDC banding criteria. Patients may have multiple lab tests because diagnostic tests may be insensitive, but are often required for treatment or insurance coverage. Twenty-two percent either reported that they do not have a positive lab test supporting their diagnosis (i.e. clinical diagnosis) or did not know (4%).



78% of patients have positive lab tests supporting diagnosis; **45%** by CDC two-tiered or western blot standards.

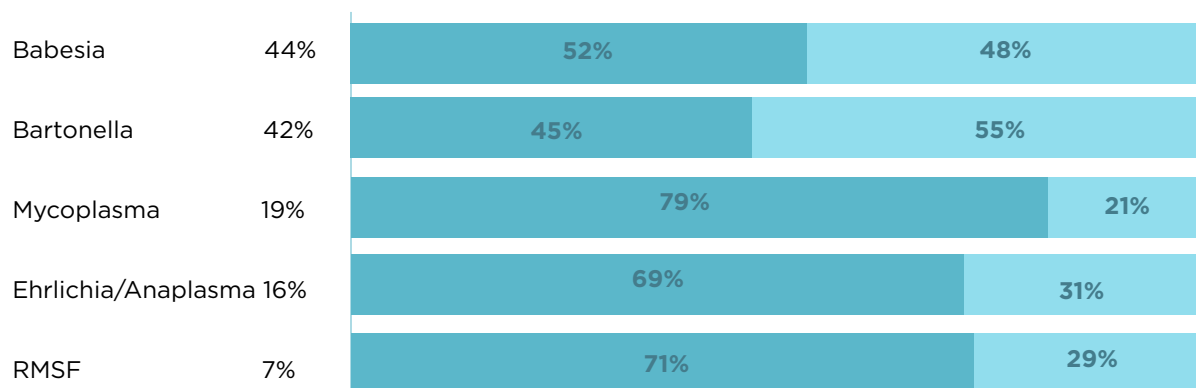
How Many Lyme Patients Test Positive?



Consistent with a prior study, co-infections appear to be common (60%). (Johnson 2014) The most frequently reported co-infections were Babesia (44%) and Bartonella (42%). Reported rates of Ehrlichia or Anaplasma were substantially lower (16%). While many coinfections were reported to have laboratory test confirmation, clinical diagnosis also plays a role. Note, however, that many physicians do not consider coinfections or may test only for select coinfections.

Co-infection Rates Are High In MyLymeData Participants

With labs | Without labs

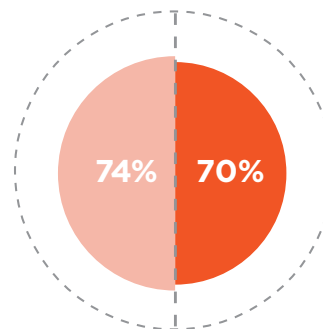


DIAGNOSIS

Avoidable Diagnostic Delays

It is generally recognized that patients who are diagnosed and treated early are more likely to become well than those diagnosed late. Unfortunately, only 12% of patients enrolled in MyLymeData were diagnosed early (within the first month), despite the fact that 74% reported having had early symptoms.*

This may be because the diagnostic hallmarks (for example, an EM rash) do not occur in many patients. Only 34% recalled having a rash. Other common sources of diagnostic delays identified included false negative lab tests (37%) and positive test results that were discarded by their healthcare provider as "false positives" (13%). Roughly half of this latter group reported that their physician disregarded their positive test report under the perception that there was no Lyme in the state where the patient resided.



74% report early symptoms;
70% are not diagnosed until late stage.

Lyme Symptoms Affect Many Systems of the Body

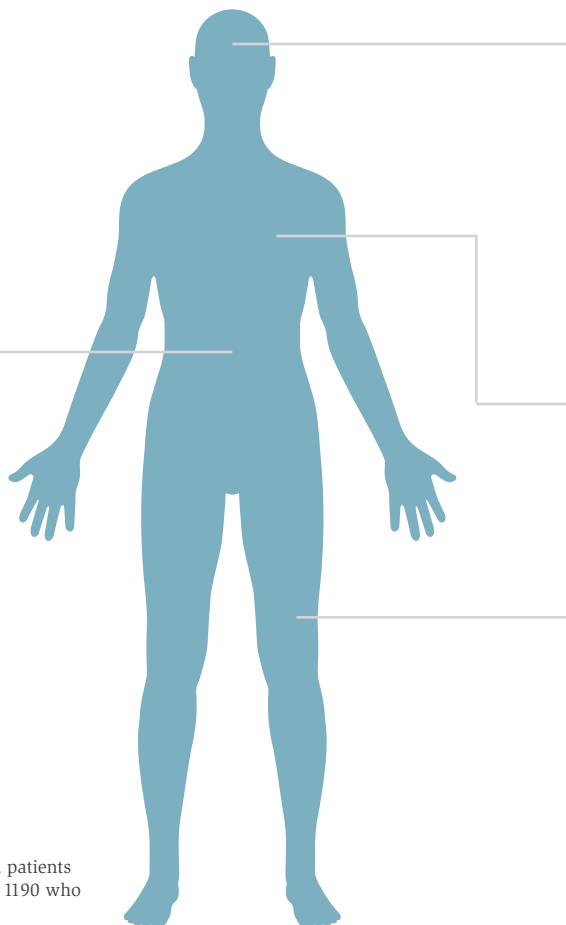
Rash

Systemic:

Flu-like Symptoms (Fever, Chills, Myalgia)
Swollen Lymph Nodes
Fatigue

Digestive:

Abdominal Pain
Nausea
SIBO
Irritable Bowel
Leaky Gut
Gastroparesis



Neurologic:

Headaches & Stiff Neck
Psychiatric
Memory Loss
Cognitive Impairment
Neuropathy (Nerve Pain or Tingling)
Bell's Palsy
Sleep Impairment

Heart:

Lightheadedness
Shortness of Breath
Heart Palpitations
Chest Pain

Musculoskeletal:

Arthritis
Muscle Aches
Joint Swelling
Joint Pain

* Because of a branching error in the initial survey, patients were re-asked this question. This data includes the 1190 who responded to the revised question.

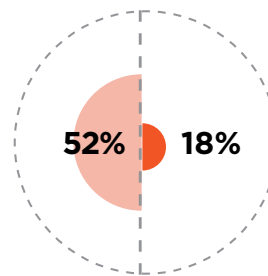
DIAGNOSIS

Misdiagnosed With Other Conditions

Delayed diagnosis (70%) is commonly reported among patients with chronic Lyme disease. Seventy-two percent of patients are misdiagnosed, almost all with diseases that offer no hope of cure. Without cure, these patients may be prescribed costly palliative (symptomatic) care for life and are at risk for the side effects associated with such symptomatic treatments.

Almost half (47%) of those misdiagnosed report that it took two or more years to correct the misdiagnosis. Although 52% are initially misdiagnosed with having a psychiatric disorder, only 18% rank psychiatric symptoms as being among their three worst symptoms.

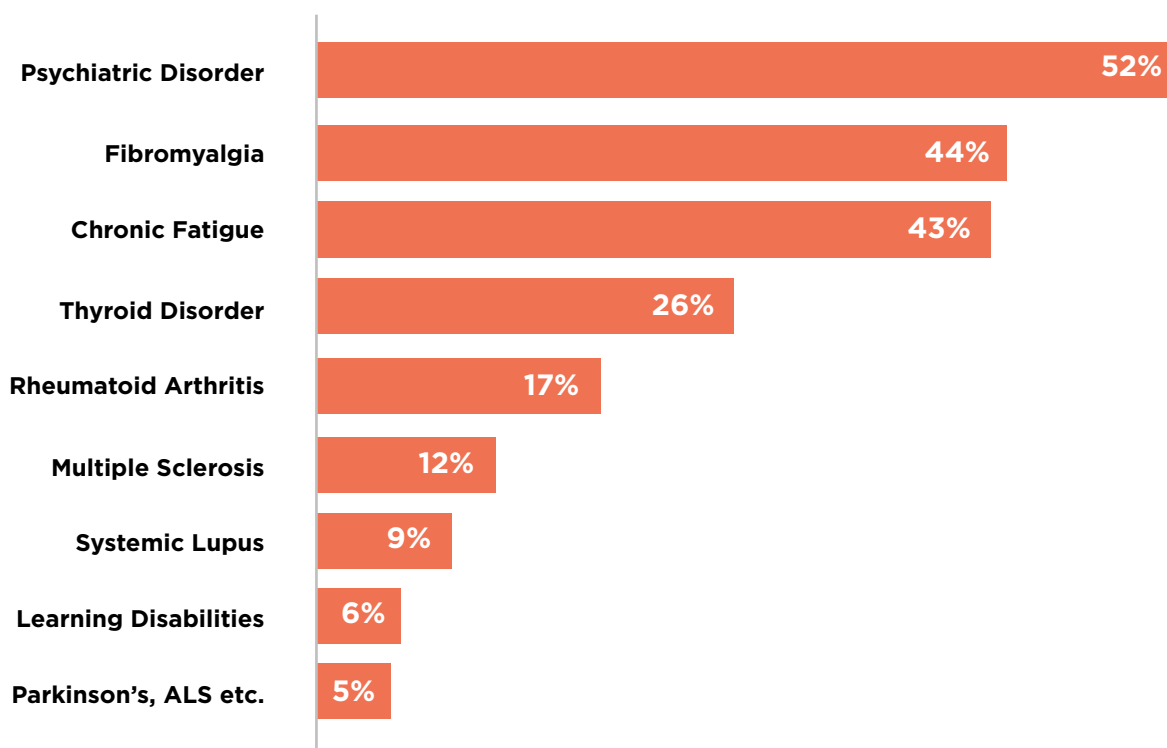
The most common misdiagnoses among those misdiagnosed include fibromyalgia (43%) and chronic fatigue (43%), thyroid disorder (26%) and rheumatoid arthritis (17%). Progressive neurologic conditions such as multiple sclerosis (12%) as well as Parkinson's disease, multiple systems atrophy, or ALS are also notable (5%).



52% were initially misdiagnosed with a psychiatric illness; but only **18%** rank psychiatric symptoms as being among their three worst.

How Is Lyme Disease Misdiagnosed?

72% of patients are misdiagnosed, almost all with diseases that offer no hope of cure.



LATE/CHRONIC SYMPTOMS

Three Worst Symptoms: Late/Chronic Lyme

We asked patients who were still ill to identify their three worst symptoms. The most frequently reported worst symptoms included neurological-associated symptoms (84%) and fatigue (62%), followed by musculoskeletal-associated symptoms (57%).

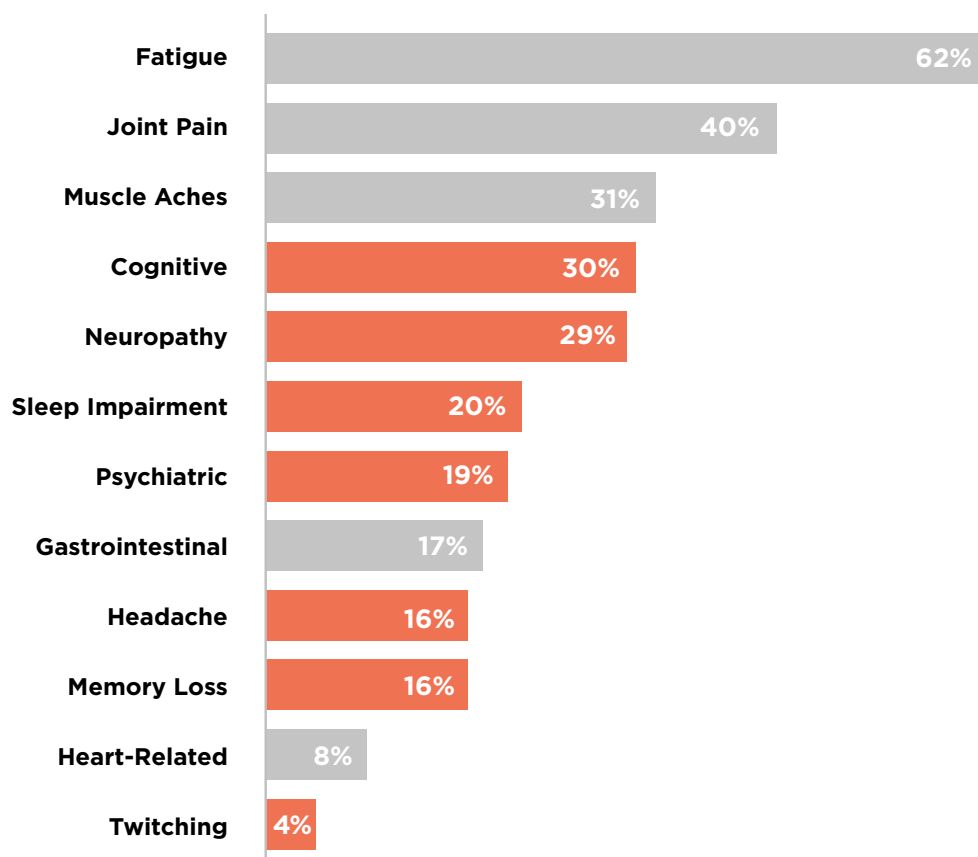


Neurologic Symptoms Are Most Frequently Reported



Neurologic symptoms included cognitive impairment, sleep impairment, memory loss, psychiatric manifestations, headaches, neuropathy, and twitching, with cognitive impairment (30%) and neuropathy (29%) most often reported among those with neurologic symptoms. Musculoskeletal symptoms included muscle aches and joint pain. The majority of patients also reported fatigue as one of their three worst symptoms.

Neurologic Symptoms are the Most Often Reported Lyme Disease Symptoms



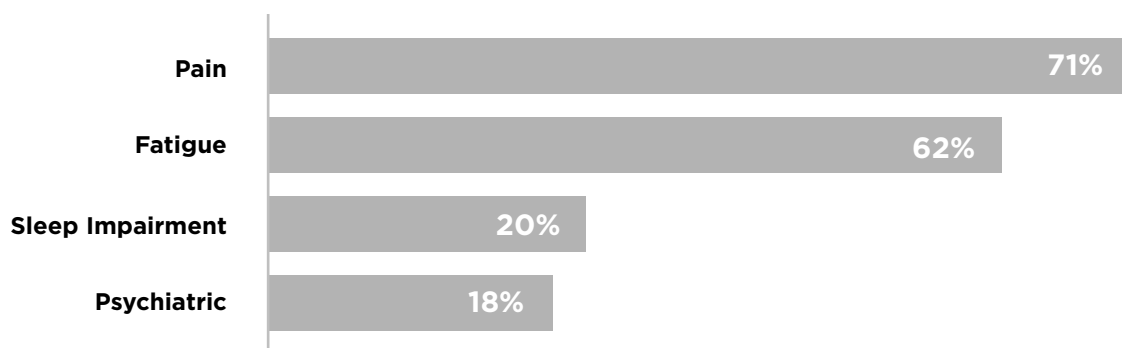
LATE/CHRONIC SYMPTOMS

Treating Symptoms

Some symptoms experienced by Lyme patients can be diminished by non-antibiotic medications used for symptomatic relief. Good examples include pain, fatigue, sleep impairment, and psychiatric symptoms. It is important to bear in mind that symptomatic relief does not address the underlying cause of symptoms. For example, pain medications may reduce pain symptoms, but do not address any underlying infection.

Many patients report taking non-antibiotic medications that address some of the symptoms identified as being among the three worst symptoms. For example, pain symptoms are common (71%) and more patients (26%) report taking prescription pain medications than the age-adjusted rate in the US general population (16%).

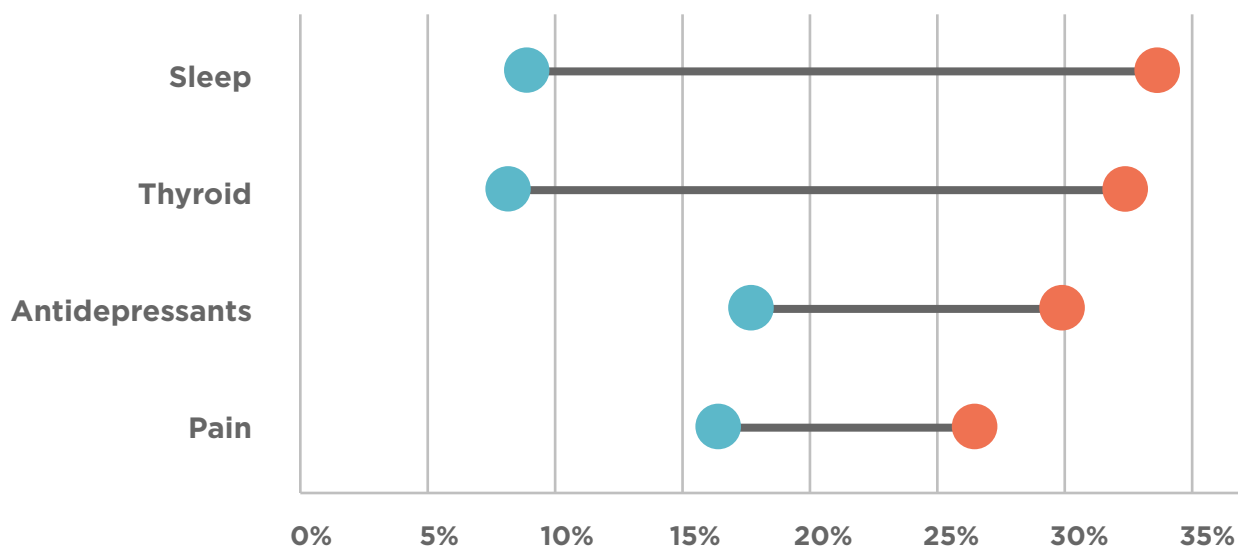
Some Symptoms That Non-Antibiotic Medications Might Alleviate



Fatigue is often reported as one of the patients' three worst symptoms (62%). Accordingly, it is not surprising that the use of thyroid medication (which can relieve fatigue in some patients) is also much higher (33%) than in the general age-adjusted population (8%). Similarly, sleep medications are taken at higher rates (34%) than the general age-adjusted population (9%) reflecting the substantial rate of sleep impairment (20%).

Chronic Lyme Disease Patients Use Symptomatic Relief Medications At Far Higher Rates Than General Population

General Population vs. MyLymeData Patients

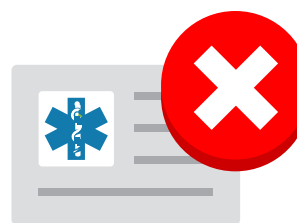


LATE/CHRONIC TREATMENT

Antibiotic Use

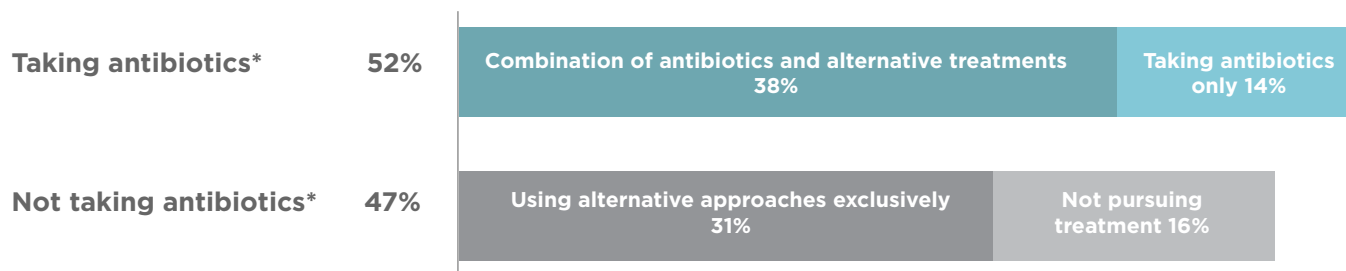
Roughly half of the patients in the registry (52%) who report being unwell are taking antibiotics, often in combination with alternative treatments (38%). Many report not taking antibiotics (47%), and 31% report using alternative treatments exclusively. Some patients (16%) report using neither alternative treatment nor antibiotics to treat their condition.

Thirty percent of those no longer taking antibiotics report that they no longer need them because they are well and 38% report that they are no longer effective.



50% report that providers do not accept insurance.

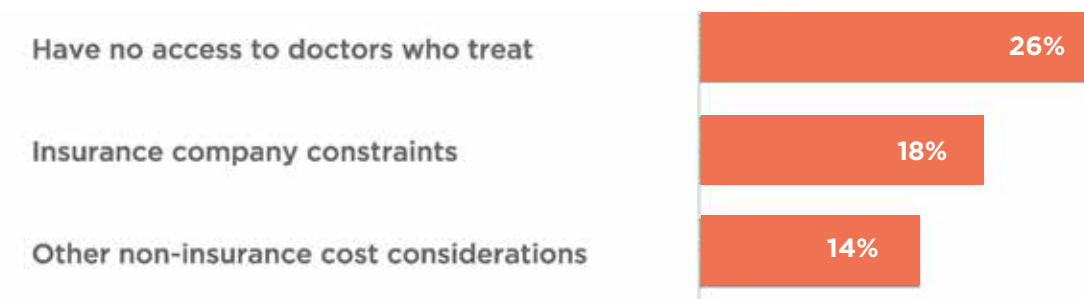
Patients using antibiotics and/or alternative treatments



* Totals do not add up to 100% due to rounding error.

Patients who are not taking antibiotics identify many reasons. However, access to physicians who treat, insurance cost constraints, and other cost factors are frequent considerations suggesting a fundamental access to care issue. Fifty percent of patients report that their treating physician does not accept insurance.

Access to care and cost considerations are major reasons patients do not use antibiotics



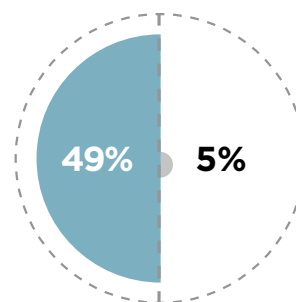
LATE/CHRONIC TREATMENT

Antibiotic Treatment

A slight majority of patients in MyLymeData (52%) report taking antibiotics to treat their Lyme disease and co-infections, with 49% reporting taking oral antibiotics and only 5% and 2% taking IV or IM antibiotics, respectively. Of those taking antibiotics, 38% report that their current antibiotic protocol is either moderately or very effective.

Thirty percent report they have been taking their current antibiotics for less than a month. Twenty-seven percent have been taking them for one to three months and 43% have been taking them longer.

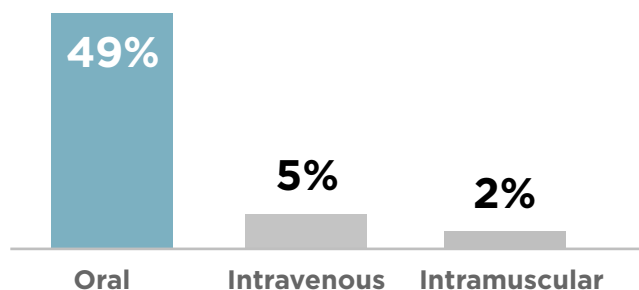
The most common oral antibiotics used are Doxycycline (36%), Zithromax (22%) and Biaxin (13%). The most common IV medications are Rocephin (59%), Zithromax (18%), and Doxycycline (13%), while the most common IM medications are Bicillin (65%) and Cleocin (20%). Thirty-five percent report that their antibiotic use is pulsed (an intermittent course of antibiotics).



49% of patients report taking oral antibiotics only;
Only 5% of patients are treated with intravenous antibiotics.

What routes of antibiotics are common?

52% of patients are being treated with antibiotics. Forty-nine percent are on oral antibiotics, 5% on intravenous, and 2% on intramuscular antibiotics.



Most Common Oral Antibiotics

- Doxycycline (Vibramycin) or Doryx
- Zithromax or Z-pak (Azithromycin)
- Biaxin (Clarithromycin)
- Minocin or Dynacin (Minocycline)
- Ceftin (Cefuroxime)
- Plaquenil (Hydroxychloroquine)
- Rifadin (Rifampin)
- Flagyl (Metronidazole)

Most Common Parenteral Antibiotics

- Rocephin (Ceftriaxone) (IV)
- Zithromax (Azithromycin) (IV)
- Doxycycline (IV)
- Flagyl (Metronidazole) (IV)
- Cleocin (Clindamycin) (IV)
- Bicillin (IM)
- Cleocin (Clindamycin) (IM)

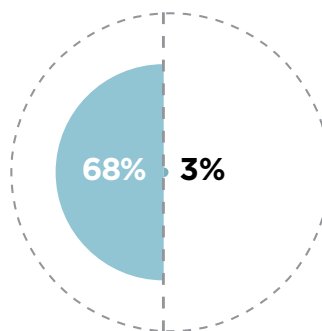
LATE/CHRONIC TREATMENT

Alternative Treatments

Patients with Lyme disease use a wide range of treatments to manage the symptoms and complications of their illness. These treatments include antibiotics, other prescription medications, and alternative treatments.

Patients who use alternative treatments either use them in conjunction with antibiotics (38 %) or as a sole means of treatment (31 %). The most popular alternative treatments included herbal protocols, sauna, chelation, and medical marijuana.

Important considerations for selecting any treatment modality include effectiveness and side effects. Herbal protocols, many of which have antimicrobial properties, are among the most popular, and 68 % of patients who used them reported that they were either moderately or very effective, with a low side effect profile.



68% rate herbal protocol effective; only **3%** rate stem cell therapy effective.

Stem cell therapy, which can be expensive, was the least popular and reported to be of limited effectiveness. Only 3 % of the 271 patients in our sample who used stem cell therapy reported that it was effective. Rife machines and chelation had the highest rate of moderate or severe side effects.

Effectiveness and side effects of alternative treatments for Lyme disease

| Response counts | | % moderate or very effective | % moderate or severe side effects |
|-----------------|--|------------------------------|-----------------------------------|
| 1,829 | Herbal protocols | 68% | 22% |
| 725 | Sauna | 65% | 17% |
| 977 | Chelation or detoxification treatments | 63% | 29% |
| 617 | Medical marijuana | 61% | 17% |
| 711 | Acupuncture | 57% | 9% |
| 848 | Homeopathy | 55% | 16% |
| 604 | Nutraceuticals | 52% | 12% |
| 509 | Electromagnetic energy therapy | 49% | 20% |
| 413 | Hypothermia or heat therapy | 45% | 19% |
| 436 | Oxygen therapies (ozone, etc.) | 40% | 14% |
| 421 | Rife Machine | 35% | 28% |
| 627 | Colloidal silver therapy | 34% | 10% |
| 347 | Hyperbaric oxygen | 22% | 13% |
| 271 | Stem cell therapy | 3% | 4% |

MyLymeData: My Data, My Trust

Patients with Lyme disease—like people with HIV/ AIDs—are often medically stigmatized and marginalized. Because of this, many are concerned about their data being used to further stigmatize, diminish, and dismiss their concerns.

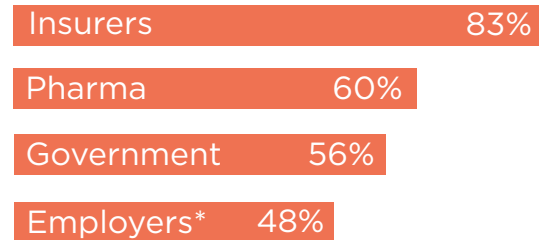
We believe that patients need to be partners in research to protect against researcher bias and ensure that patient data is used to benefit the interests of patients.

We surveyed over 1,900 patients enrolled in the MyLymeData registry on the topic of privacy, data use, trust, discrimination and stigma. (Johnson 2019) Most reported that MyLymeData's role as a community steward, vetting researchers and the use of data, was important in their decision to participate in the study.

Patients in the survey had many concerns about the potential misuse of their data.

- 80% worried that an insurer might use their healthcare data to deny coverage in the future as a pre-existing condition;
- 48% of those employed worried that employers might use healthcare data to limit their career opportunities;
- Respondents worried about the use of their health data by the government (56%), pharmacies (49%), and drug companies (60%);

Lyme Patients Worry About Use of Their Data By:



*Includes only those employed or looking for work.

We believe that community-based data stewardship is required to protect individual Lyme patients and the Lyme disease community from harm. Although MyLymeData was initially part of PCORnet, the big data project of the Patient Centered Outcomes Research Institute, we withdrew from that project prior to launch to protect the community from unrestricted data use policies.

Accordingly, we vet researchers and restrict data use and re-use to ensure that patient data is used solely for the benefit of Lyme disease patients.

We protect patients by providing researchers with access to de-identified data only and by prohibiting unauthorized re-identification.

We require researchers to limit access to the data, encrypt the data and maintain it securely.

Many big data projects sell data to third parties like pharma or insurers. We do not. Our commitment is to make sure that patient data is used for the benefit of patients—period.



Patient-Centered Privacy

- Obtain patient consent to share data.
- Share only what is needed.
- Share only for the benefit of patients.
- Tell patients who is using their data and why.
- Keep data secure.

Cost Of Illness

Early diagnosis and treatment is essential to reduce the rate of late/chronic Lyme disease. Unfortunately—at least among those with late/chronic Lyme disease (79 % of patient enrolled in the registry)—it appears to be more the exception than the rule. Only 12 % report being diagnosed in the first month. Early diagnosis and treatment is effective for most patients, but the majority of those with late/chronic Lyme disease (88 %) are not diagnosed early. This presents an opportunity to prevent patients from developing Lyme disease through early diagnosis.

Lyme disease significantly impairs patient quality of life, making it difficult for patients to work, go to school, and engage in everyday activities. Compared to the general population and patients with other chronic diseases, patients with late/chronic Lyme disease have

significantly lower health quality status, more bad mental and physical health days, a significant symptom disease burden, and greater activity limitations. (Johnson 2014) Roughly a third (32 %) of those in MyLymeData report their work status as disabled (whether or not receiving disability payments).

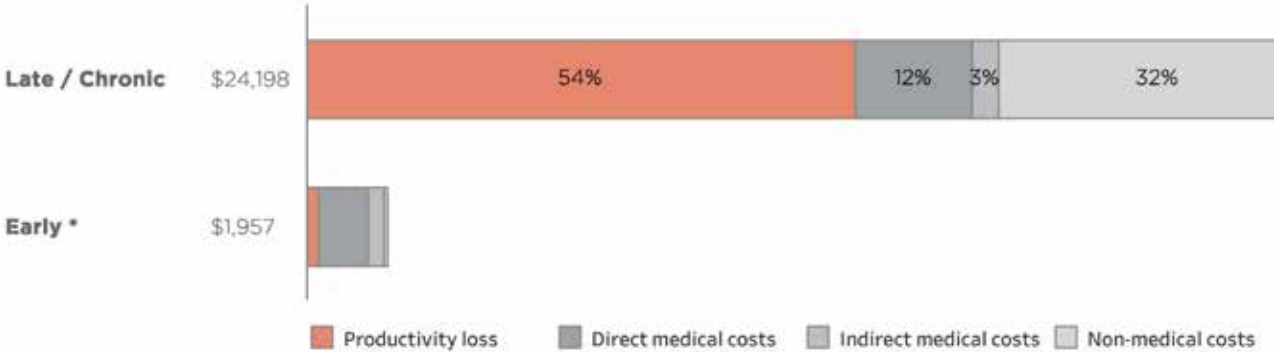
According to a study by Dr. X. Zhang of the CDC, the cost of treating late/chronic Lyme disease is over 12 times higher than the cost of treating early Lyme disease. His study focused on capturing all societal costs regardless of who made payment for the costs. Hence, the study included direct medical costs, indirect medical costs (e.g. additional out-of-pocket medications), other costs (e.g. travel), and costs due to loss of productivity (e.g. lost work days).

| Lyme Disease Cost Per Patient for Early vs Late Lyme Disease | | | | |
|--|-------------------|--------------------------|-------------------|--------------------------|
| Year | 2000 Dollars | | 2018 Dollars | |
| | Early LD \$\$ (%) | Late/chronic LD \$\$ (%) | Early LD \$\$ (%) | Late/chronic LD \$\$ (%) |
| Direct medical | \$801 (61%) | \$1,872 (12%) | \$1,196 (61%) | \$2,796 (12%) |
| Indirect medical | \$259 (20%) | \$434 (3%) | \$387 (20%) | \$648 (3%) |
| Non-medical | \$52 (4%) | \$5,109 (32%) | \$78 (4%) | \$7,631 (32%) |
| Productivity loss | \$198 (15%) | \$8,785 (54%) | \$296 (15%) | \$13,123 (54%) |
| Total | \$1,310 | \$16,200 | \$1,957 | \$24,198 |
| (Zhang 2006) https://data.bls.gov/cgi-bin/cpicalc.pl?cost1=198&year1=200001&year2=201808 | | | | |

The graph below shows the dramatic difference between the costs per case for early Lyme disease compared to late/chronic Lyme disease. Most of the increased cost is due to productivity losses associated with reduced health status.

Late/Chronic vs. Early Lyme Disease Cost Comparison

Late/chronic Lyme disease costs are **12 times higher** than early Lyme disease costs with costs due to productivity loss accounting for more than half the costs.



A more recent Johns Hopkins study by Adrion, using a big data insurance base, found direct medical costs to be \$2,968 higher for patients with early Lyme disease. Adrion's costs looked only at patients with early Lyme disease. It considered all direct medical costs, but excluded all other costs (e.g. indirect medical costs and loss of productivity).

Zhang estimated that in 2000 dollars, the annual cost of Lyme disease in the US was \$203 million. With the CDC's increased estimate of annual Lyme cases (from 30,000 to 300,000) as well as adjustment for inflation, these costs have increased substantially.

Adrion's study concluded that Lyme disease direct medical costs for early Lyme disease alone may be as high as \$1.3 billion a year. Assuming the same indirect medical costs, non-medical costs and productivity loss percentages as Zhang, would increase the annual cost of early Lyme disease in the study by 39% to \$4,125 per patient or \$1.8 billion a year when applied to CDC case estimates.

However, the total costs of Lyme disease consist of both the costs of early and late/chronic Lyme disease. The number of patients with chronic or persistent Lyme disease is unknown, but may be estimated based on the stage of the disease at diagnosis and the percentage of treatment failures associated with that

stage. Treatment failures ranging from 10-35% have been reported in early disease and higher rates are reported for late disease. Prevalence of late/chronic Lyme disease is a cumulative number that grows annually and is diminished only by death or cure. Unfortunately, these patients may remain ill for a very long time. In one study, nearly half of the sample reported having had Lyme disease for more than 10 years, perhaps a lifetime. (Johnson 2014)

The table below is based on the CDC 300,000 annual case estimates and treatment failure rates ranging from 10% to 50%. The percentage of patients who fail treatment is then used to estimate the cumulative number of those who remain ill over time.

Assuming that between 35 and 50% remain ill after treatment and the duration of their illness lasts between 10 and 20 years, persistent Lyme disease would range from 1 to 3 million cases.

This would place the total annual cost of late/chronic Lyme disease based on 24,198 per case at roughly between \$24 and \$72 billion dollars. When the total costs (direct medical, indirect medical, non-medical, and loss of productivity costs) of acute (\$1.8 billion) and late/chronic Lyme disease are combined, they aggregate to between \$25.8 to \$73.8 billion.

| Number of Late/Chronic Lyme Disease Patients Over Time | | | | | |
|--|-----------|--|-----------|------------------|------------------|
| Year | Incidence | Treatment Failure Rate for Late/Chronic Lyme | | | |
| | | 10% | 20% | 35% | 50% |
| 1 | 300,000 | 30,000 | 60,000 | 105,000 | 150,000 |
| 5 | 300,000 | 150,000 | 300,000 | 525,000 | 750,000 |
| 10 | 300,000 | 300,000 | 600,000 | 1,050,000 | 1,500,000 |
| 15 | 300,000 | 450,000 | 900,000 | 1,575,000 | 2,225,000 |
| 20 | 300,000 | 600,000 | 1,200,000 | 2,100,000 | 3,000,000 |

Early diagnosis and treatment restores most patients to health and reduces the number of patients who progress to late/chronic Lyme disease—which, in turn, reduces medical and societal costs of the disease. This is a winnable battle, but it requires that barriers to early diagnosis (absence of a rash, failure to recognize the growing geographic expansion of the disease, and the inadequacy of current laboratory tests) be acknowledged and addressed.

Publications, Collaborations, Presentations

Publications and Preprints:

Johnson L, Shapiro M, Mankoff J. Removing the Mask of Average Treatment Effects in Chronic Lyme Disease Research Using Big Data and Subgroup Analysis. *Healthcare*. 2018;6(4):124. Available from: <http://www.mdpi.com/2227-9032/6/4/124>.

Abstract: This study uses a big data sample of 3,903 from MyLymeData to examine variations in individual treatment response compared to average treatment effects. While treatment average effects reveal little response to treatment, individual treatment response varied widely. More than half (52%) reported at least some improvement, with 34% saying that they improved “moderately” to “a very great deal.” Slightly more than a third (37%) had no treatment response. Only 12% reported that their symptoms were worse after treatment.

Johnson, Lorraine (2019): Stigma and Privacy in Lyme Disease [Preprint]. <https://doi.org/10.6084/m9.figshare.7704167>.

Abstract: Between November 5, 2018 and February 2, 2019, the MyLymeData patient registry conducted a survey of over 1,900 patients enrolled on the topic of privacy, data use, trust, discrimination and stigma. (Johnson 2019) Most patients (78%) said that they are concerned about privacy in Lyme disease. Roughly half of respondents worried about the use of their health data by the government (56%) and pharmacies (49%), with a higher number expressing such concern about drug company data use (60%).

Over 80% worried that an insurer might use their healthcare data to deny coverage in the future as a pre-existing condition. Approximately half of those employed (48%) were concerned that employers might use healthcare data to limit their career opportunities. Patients also worried about data use and research bias. Most patients (84%) reported that MyLymeData’s role as a community steward vetting researchers and the use of data was important in their decision to participate in the study.

Collaborations and Researcher Engagement:

MyLymeData collaborates with academic researchers at the University of California at Los Angeles and at the University of Washington. The National Science Foundation

has funded UCLA researchers to explore big data analytics using data from the registry using predictive analytics to determine diagnostic risk and treatment factors.

We are also collaborating on a tissue collection project with the leading source for research tissues in the nation, the National Disease Research Interchange, and the Bay Area Lyme Foundation Tissue Bank. This collaboration permits patients donating tissues to enroll in MyLymeData and connect their data with tissue samples donated to the project.

Presentations:

Johnson L. Building a Research Engine with MyLymeData [Key Note Presentation]. U.S. Health and Human Services. Lyme Innovation Roundtable; December 4, 2018; Washington, DC.

Johnson, L. From Misdiagnosis to Patient-Driven Research: MyLymeData. [Plenary Presentation] Society to Improve Diagnosis in Medicine. New Orleans. November 3, 2018.

Johnson, L. Access to Care: Measuring what matters. [Webinar] Health and Human Services—Tick Borne Diseases Working Group, Access to Care Subcommittee May 2, 2018.

Johnson, L. Patient-Centered Lyme Disease Research & Big Data. [Plenary Presentation] Health and Human Services—Tick Borne Diseases Working Group, Washington, DC. December 11, 2017.

Johnson, L. MyLymeData: The Value of Using Big Data and Subgroup Analysis in Lyme Disease. [Plenary Presentation] Columbia/LDA Conference, Philadelphia. September 24th, 2017.

Johnson, L. Using a New Patient Powered Research Tool to Answer Critical Questions About Lyme Disease. [Plenary Presentation] International Lyme and Associated Diseases Society Annual Meeting. Philadelphia. November 5, 2016.

Johnson, L. Patient Powered Research. American Association for the Advancement of Science. Washington, DC. February 14, 2016.

Johnson, L. Precision Medicine Initiative Summit. [Participant] White House, February 25, 2016. Washington, DC.

Johnson, L. Patient Powered Research. [Ignitor Presentation] Stanford MedX Conference. Stanford, CA. September 26, 2015.



National Science Foundation
WHERE DISCOVERIES BEGIN



Using a New Patient-Powered Research Tool to Answer Critical Questions about Lyme Disease

Lorraine Johnson, Phyllis Mervine, Melissa Potter
LymeDisease.org, Los Angeles, CA USA

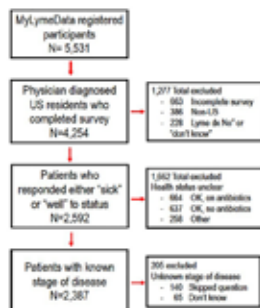
Introduction

MyLymeData is a patient registry developed by LymeDisease.org that enables patients to pool longitudinal healthcare data. Since its launch in November 2015, 5,531 patients have enrolled.

The 4,254 participants in this sample included US residents clinically diagnosed with Lyme disease who completed the survey. A subgroup that characterized themselves as “sick” (86%) or “well” (14%) and identified the stage of their disease at diagnosis (2,387) was analyzed.

We compare the recovery rate of the 21% diagnosed early with the 79% diagnosed late (untreated for 6 months or more after onset).

Sample & exclusions algorithm

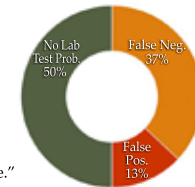


Results

Patients diagnosed early were more likely to be “well” (32%) than patients diagnosed late (9%). Still, a large proportion of patients diagnosed early (68%) and almost all of those diagnosed late (91%) remained ill. These findings suggest the importance of early diagnosis and the need to develop improved treatment regimens for both early and late Lyme disease.

| Early or Late Diagnosis and Recovery in Lyme Patients | | | |
|---|------------|--------------|--------------|
| | Early | Late | Total |
| Sick | 343 (68%) | 1,721 (91%) | 2,064 (86%) |
| Well | 159 (32%) | 164 (9%) | 323 (14%) |
| Total | 502 (100%) | 1,885 (100%) | 2,387 (100%) |

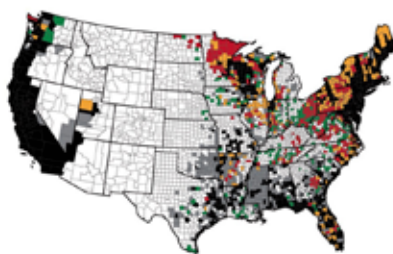
Causes of diagnostic delays



Diagnostic delays were associated with false negative lab tests (37%), positive lab tests dismissed as “false positives” (13%), and missed diagnostic opportunities when healthcare providers failed to evaluate the patient because “there is no Lyme here.”

Widely varying estimates from different sources of information in states regarded as non-endemic suggest the true incidence/prevalence of Lyme disease is too uncertain to prematurely foreclose clinical diagnosis based on predictive modules, such as Bayes’ Theorem. The CDC acknowledges case reports underestimate actual incidence by a factor of 10 nationwide.

Traditional maps highlighting risk of Lyme disease by state can be misleading. For example, most maps including the one below, reflect the geographic distribution of ticks where tick flagging studies have been conducted. Unfortunately, most counties have not conducted tick flagging studies.



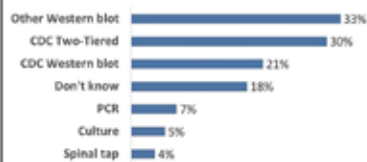
Indicators of true incidence of Lyme disease in Colorado vary widely.

| Source | # of Cases |
|---|------------|
| CDC cases (1994-2014) | 12 |
| 10X multiplier of CDC cases | 120 |
| MILD cases (launch Nov 2016) | 85 |
| MILD tick bites | 23 |
| ILADS physician referral requests (2014-16) | 742 |
| Canine cases (rolling 5 years) | 515 |

Black/grey: reported before 1996. Red/green/yellow: new reports 1996-2015. Eisen et al. J Med Entomol. Jan 2016

Supporting Diagnostic Tests

Most patients (78%) enrolled in MyLymeData report their diagnosis is supported by positive lab tests.



Conclusions

Lyme disease patients have significantly better outcomes when they are diagnosed early. Reducing barriers to diagnosis and improving treatments should be a public health priority. Physicians should be advised that lab tests are insensitive and may give false negative results. Patients with an erythema migrans rash should be promptly treated without lab testing as false negative test results at this stage are typical. Positive test results should not be discounted in symptomatic patients. Public health officials should be aware that CDC case numbers may greatly underestimate the true incidence of Lyme disease in an area. Finally, even in areas where Lyme disease is less common, symptomatic patients need to be tested and accurately diagnosed to prevent unnecessary suffering. It is time to focus on prompt diagnosis and early intervention to prevent chronic Lyme disease from developing.

Limitations and Future Research

This analysis is correlational and cannot determine cause and effect. We do not examine treatment effects. Future studies might explore the association between treatment and restoration of health.

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Further Information

For further information about this poster session or MyLymeData, please contact Lorraine Johnson, CEO, LymeDisease.org. MyLymeData can assist researchers in many ways, for example, by providing patient registry data; collecting new survey data; recruiting patients for studies; and providing long term follow-up for completed trials.

Literature cited

Canine cases: IDEXX Laboratories. Canine Vector-Borne Disease Prevalence Map (Rolling 5 years). <http://www.idexx.com/canine-vector-borne-disease-prevalence-map>
Centers for Disease Control and Prevention. 2000-2014 (8 cases). <http://www.cdc.gov/ncez/lyme-disease/>
1990-2001 (4 Cases). <http://www.cdc.gov/ncez/lyme-disease/>

CDC News (2016) Lyme Disease Diagnoses Difficult in Colorado. <http://www.cdc.gov/media/releases/2016/s0601-lyme-disease-diagnoses.html>
MyLymeData: Registrants residing in Colorado enrolled since registry launched November 12, 2015.

MyLymeData: Registrants enrolled since registry launched November 12, 2015 who recall and identify tick bite location as Colorado.

International Lyme and Associated Diseases Society. Results of Physician Referral Analysis (personal correspondence.)



References

- Adrion ER, Aucott J, Lemke KW, Weiner JP. Health care costs, utilization and patterns of care following Lyme disease. *PLoS ONE*. 2015;10(2):e0116767. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/25650808>.
- Aucott J, Morrison C, Munoz B, Rowe PC, Schwarzwald A, West SK. Diagnostic challenges of early Lyme disease: lessons from a community case series. *BMC Infect Dis*. 2009;9:79. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19486523>.
- Blackwell DL, Lucas JW, TC. C. Summary health statistics for U.S. adults: National Health Interview Survey, 2012. . *Vital Health Stat* 10(260) 2014. 2014. Available from: https://www.cdc.gov/nchs/data/series/sr_10/sr10_260.pdf
- Centers for Disease Control and Prevention. Lyme Disease--United States, 1992-2006. *MMWR*, 2008; 57((10)). Available from: <https://www.cdc.gov/mmwr/pdf/ss/ss5710.pdf>.
- Clinical and Translational Science Awards Consortium. Community Engagement Key Function Committee. Task Force on the Principles of Community Engagement., United States. Department of Health and Human Services., National Institutes of Health (U.S.), Centers for Disease Control and Prevention (U.S.), United States. Agency for Toxic Substances and Disease Registry. Principles of community engagement. Second edition.
- Department of Health and Human Services, Maine Center for Disease Control and Prevention, Report to Maine Legislature: Lyme Disease. 2010.
- Davis K, Collins S, Doty M, Ho A, Holmgren A. Health and Productivity Among U.S. Workers. The Commonwealth Fund Issue Brief 856. 2005. Available from: https://www.commonwealthfund.org/sites/default/files/documents/___media_files_publications_issue_brief_2005_aug_health_and_productivity_among_u_s_workers_856_davis_hlt_productivity_usworkers.pdf
- Fallon, B.A.; Keilp, J.G.; Corbera, K.M.; Petkova, E.; Britton, C.B.; Dwyer, E.; Slavov, I.; Cheng, J.; Dobkin, J.; Nelson, D.R.; et al. A randomized, placebo-controlled trial of repeated iv antibiotic therapy for Lyme encephalopathy. *Neurology* 2008, 70, 992–1003.
- Fallon BA, Kochevar JM, Gaito A, Nields JA. The underdiagnosis of neuropsychiatric Lyme disease in children and adults. *Psychiatr Clin North Am*. 1998 Sep;21(3):693-703, viii. Available from: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=9774805
- Gliklich, R.D.N.; Leavy, M. (Eds.) Registries for Evaluating Patient Outcomes: A User's Guide, 3rd ed.; Agency for Healthcare Research and Quality: Rockville, MD, USA, 2014.
- Groft, S. Patient Registries As a Prelude to Clinical Trials and Post-Approval Studies; Pediatric Devices for Rare Diseases Food and Drug Administration: White Oak, MD, USA, 8 January 2014.
- Henry J. Kaiser Family Foundation, Percent of Adults Reporting Fair or Poor Health Status. Available from <https://www.kff.org/other/state-indicator/percent-of-adults-reporting-fair-or-poor-health-status/?currentTimeframe=0&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D>
- Johnson, Lorraine (2019): Stigma and Privacy in Lyme Disease [Preprint]. <https://doi.org/10.6084/m9.figshare.7704167>
- Johnson L, Shapiro M, Mankoff J. Removing the Mask of Average Treatment Effects in Chronic Lyme Disease Research Using Big Data and Subgroup Analysis. *Healthcare*. 2018;6(4):124. Available from: <http://www.mdpi.com/2227-9032/6/4/124>.
- Johnson L, Aylward A, Stricker RB. Healthcare access and burden of care for patients with Lyme disease: a large United States survey. *Health Policy*. 2011 Sep;102(1):64-71. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/21676482>.
- Johnson L, Wilcox S, Mankoff J, Stricker RB. Severity of chronic Lyme disease compared to other chronic conditions: a quality of life survey. *PeerJ*. 2014; 2. Available from: <http://dx.doi.org/10.7717/peerj.322>.
- Klempner, M.; Hu, L.; Evans, J.; Schmid, C.; Johnson, G.; Trevino, R.; Norton, D.; Levy, L.; Wall, D.; McCall, J.; et al. Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. *N. Engl. J. Med*. 2001, 345, 85–92.
- Kravitz RL, Duan N, Braslow J. Evidence-based medicine, heterogeneity of treatment effects, and the trouble with averages. *Milbank Q*. 2004;82(4):661-87.
- Krupp, L.B.; Hyman, L.G.; Grimson, R.; Coyle, P.K.; Melville, P.; Ahnn, S.; Dattwyler, R.; Chandler, B. Study and treatment of post Lyme disease (Stop-LD): A randomized double masked clinical trial. *Neurology* 2003, 60, 1923–1930.
- National Center for Health Statistics. Health, United States, 2016 with Chartbook on Long-term Trends in Health. Hyattsville, MD. 2017. Available from: <https://www.cdc.gov/nchs/data/hsr/hsr16.pdf>.
- Stricker RB, Fessler M. Chronic Lyme Disease: A Working Case Definition. *American Journal of Infectious Diseases*. 2018;14(1):1-44. Available from: <http://thescipub.com/pdf/10.3844/ajidsp.2018.1.44>
- Wormser GP, Dattwyler RJ, Shapiro ED, Halperin JJ, Steere AC, Klempner MS, et al. The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. *Clin Infect Dis*. 2006 Nov 1;43(9):1089-134.
- Zhang, X., et al., Economic impact of Lyme disease. *Emerg Infect Dis*, 2006. 12(4): p. 653-60.



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