Using Patient Registry Data to Assess Enrollment Criteria in Lyme

MyLymeData

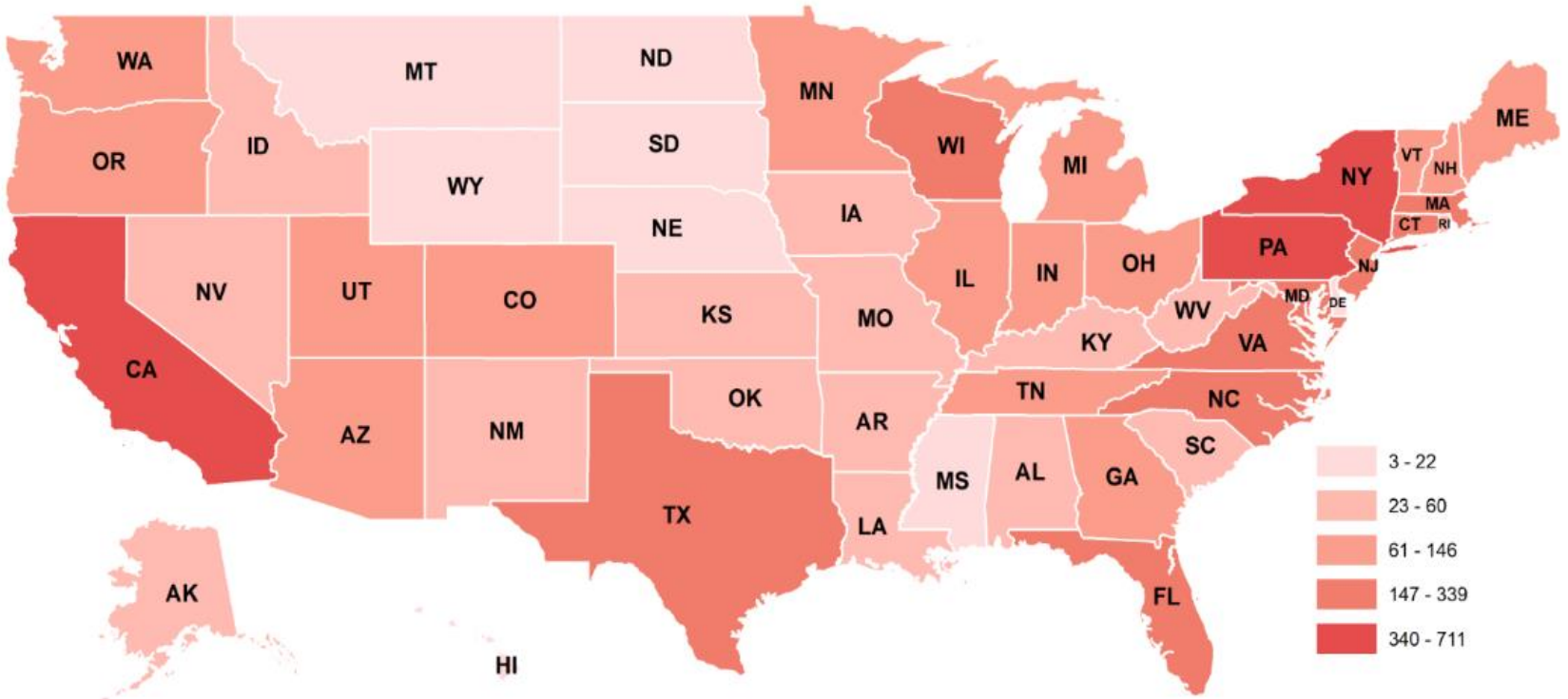
A PROJECT OF LYMEDISEASE.ORG

Toward a Common Research Agenda in Infection-Associated Chronic Illnesses June 30, 2023

Lorraine Johnson, JD|MBA • PI MyLymeData • CEO, LymeDisease.org

MyLymeData Patient Registry

Over 17,000 enrolled



Publications

Johnson L, Shapiro M, Stricker RB, Vendrow J, Haddock J, Needell D. Antibiotic Treatment Response in Chronic Lyme Disease: Why Do Some Patients Improve While Others Do Not? Healthcare. 2020; 8(4):383. https://doi.org/10.3390/healthcare8040383

Vendrow J, Haddock J, Needell D, Johnson L. Feature Selection from Lyme Disease Patient Survey Using Machine Learning. Algorithms. 2020; 13(12):334. https://doi.org/10.3390/a13120334

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. https://doi.org/10.3390/healthcare6040124

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:e322. Published 2014 Mar 27. doi:10.7717/peerj.322

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;102(1):64-71. https://doi.org/10.1016/j.healthpol.2011.05.007

What information does MyLymeData collect?

Diagnosis validation questions:

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

Diagnosis

- Recollection of tick bite
- Diagnosis by clinician
- Supporting lab tests
- Stage of illness at diagnosis

Demographics

- Sex
- Race
- Education
- State of residence

Quality of Life

- Health status
- Bad physical days
- Bad mental days
- Bed days

Functional Impairment

- Ability to work
- Ability to go to school
- Impact on social activities
- Disability

Treatments

- Antibiotics
- Alternative
- No treatment
- Treatment duration

Symptoms

- Severity
- Present at diagnosis
- Most Common
- Percent of Improvement

(Gliklich, AHRQ 2014)

Patient generated data is the most complete Real World Data

Patient-generated data excels because the information is:

- Designed for registry research (not EHR and claims system artifacts)
- The most complete data (cross silo)
- Data that only patients may know
- Includes patients outside the insurance system (roughly 50%)
- Not limited by single center geographic, practice-based constraints, or research study limits

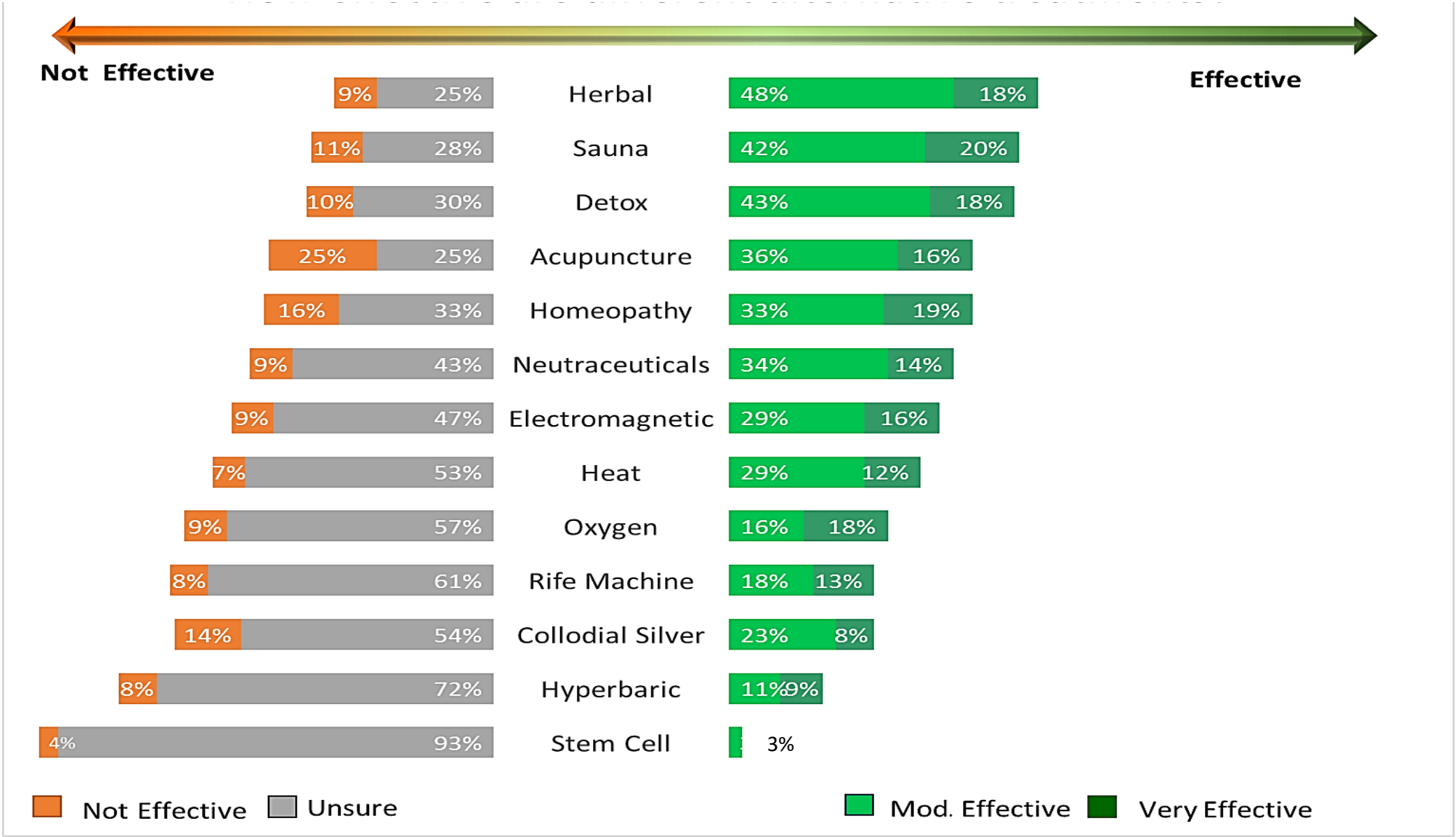
---

Patient registries excel at:

- Characterizing the disease and patient populations
- Identifying subgroups
- Defining patient centered outcomes and endpoints
- Assessing treatment effectiveness
- Capturing patient treatment innovation

What are the most effective alternative treatments?

N=2326

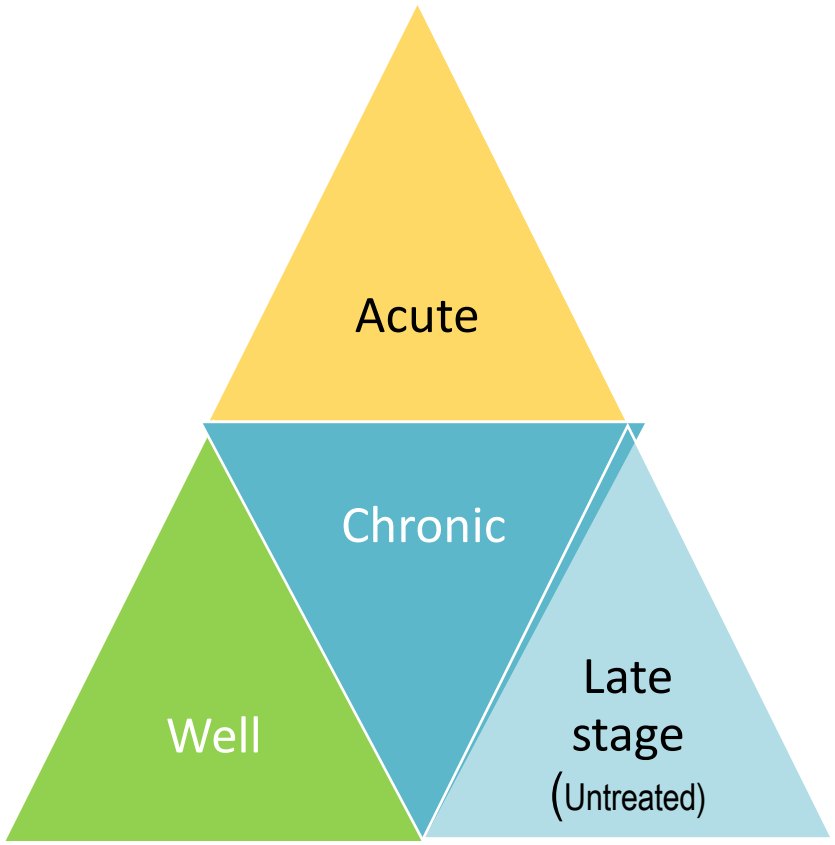


N=271

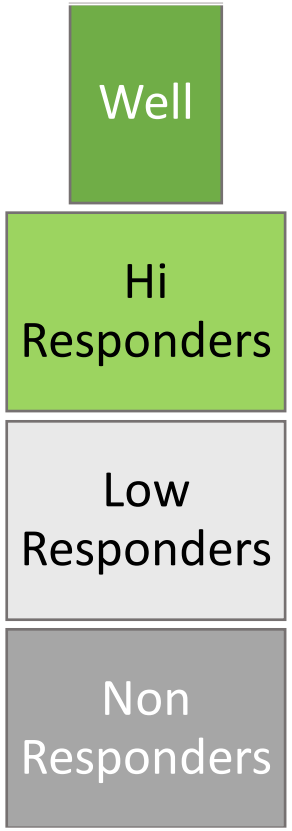
Phase 1 Data Set, MyLymeData (November 2016)

Important patient subgroups in Lyme disease

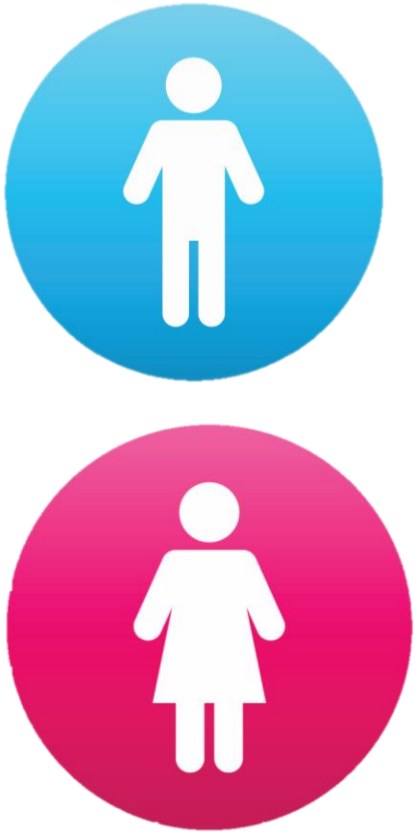
Stage/ status of disease



Treatment responders



Biological sex



Symptom Severity

Fatigue
Joint Pain
Muscle Aches
Cognitive
Neuropathy
Sleep Impairment
Psychiatric
Gastrointestinal
Headache
Memory Loss
Heart-Related
Twitching

Using MyLymeData to assess the effect of exclusion criteria

- Research question: How do commonly used research enrollment criteria impact attrition and sample enrollment yield in persistent Lyme disease?

- Sample size 2000 patients with persistent Lyme disease enrolled in MyLymeData

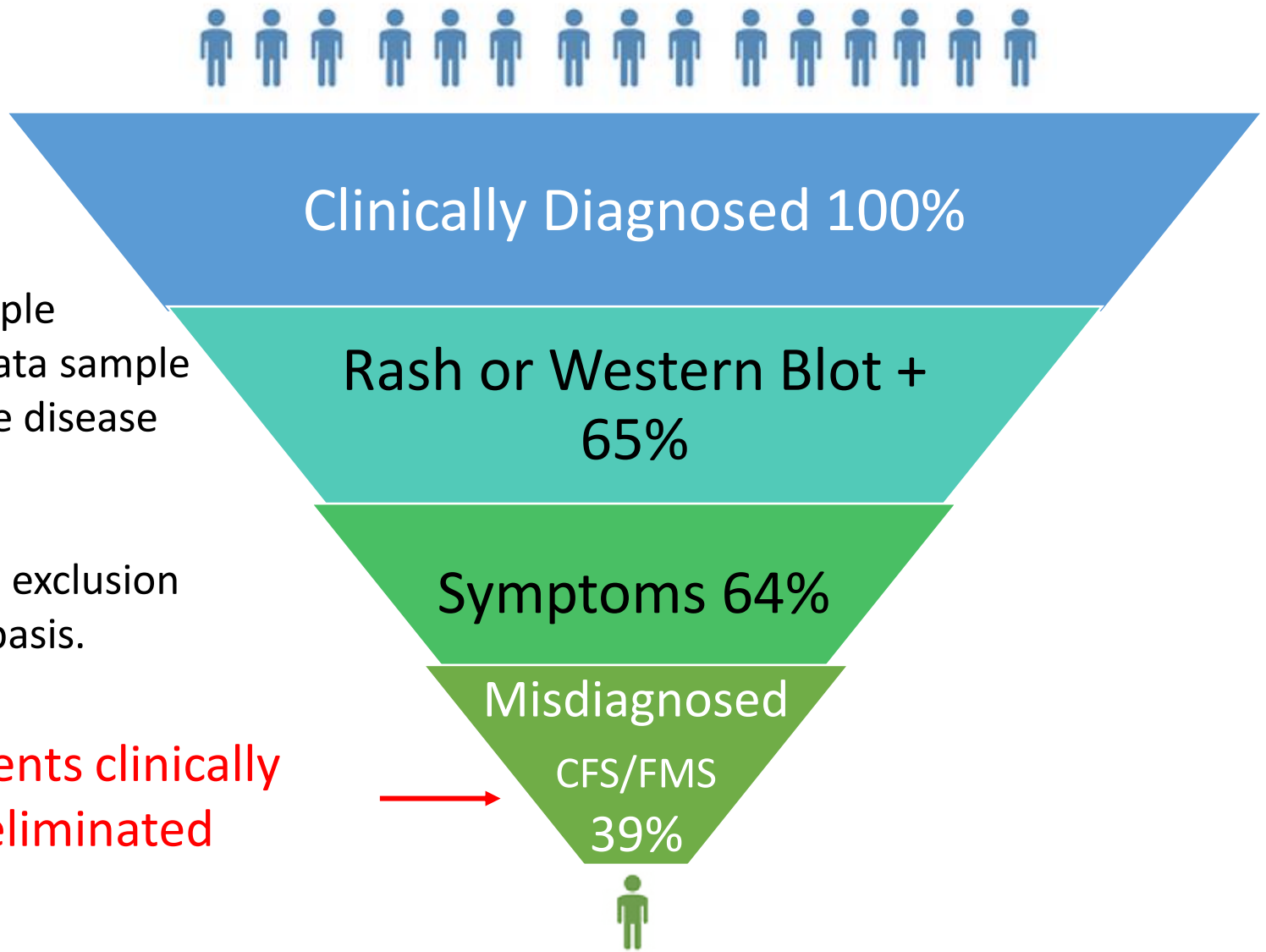
- We looked at 4 common research enrollment criteria:
    - Positive Western blot
    - History of a rash
    - Symptoms and severity of symptoms
    - No diagnosis of ME/CFS or FMS

Sample attrition for persistent Lyme based on exclusion criteria

Use case example of sample attrition using MyLymeData sample of >2,396 persistent Lyme disease patients

Applying commonly used exclusion criteria on a cumulative basis.

61% of patients clinically diagnosed eliminated



Unpublished data Johnson 2023

RCTs use narrower enrollment criteria and exclude more patients

Research definition exclusions can:

- Affect the generalizability of results
- Increase the time to recruit
- Increase the cost of research
- Randomized controlled trials use more narrow criteria for enrollment which reduces sample yield further
  - For example, NIH Lyme treatment trials excluded 89-99% of those who sought to enroll

	Screened	Enrolled	Yield	Time to Recruit
Klempner	1966	129	7%	3.3 years
Krupp	512	56	11%	2.5 years
Fallon	3368	37	1%	4 years

89-99% of patients eliminated

Klempner (2001), Krupp (2003), Fallon (2008)

Calls to relax enrollment criteria in clinical trials

Expanding Access to Lung Cancer Clinical Trials by Reducing the Use of Restrictive Exclusion Criteria: Perspectives of a Multistakeholder Working Group

Eligibility Criteria of Randomized Controlled Trials Published in High-Impact General Medical Journals
A Systematic Sampling Review

Journal of Clinical Psychopharmacology

Articles & Issues | Collections | Podcasts | Blog | For Authors | Journal Info

ORIGINAL CONTRIBUTIONS

Are Participants in Pharmacological and Psychotherapy Treatment Trials for Social Anxiety Disorder Representative of Patients in Real-Life Settings?

Hoertel, Nicolas MD, MPH*†‡; de Maricourt, Pierre MD†‡§; Katz, Julien MD‖; Doukhan, Raphaël MD¶; Lavaud, Pierre MD*†; Peyre, Hugo MD, MPH¶#; Limosin, Frédéric MD, PhD*†‡

nature

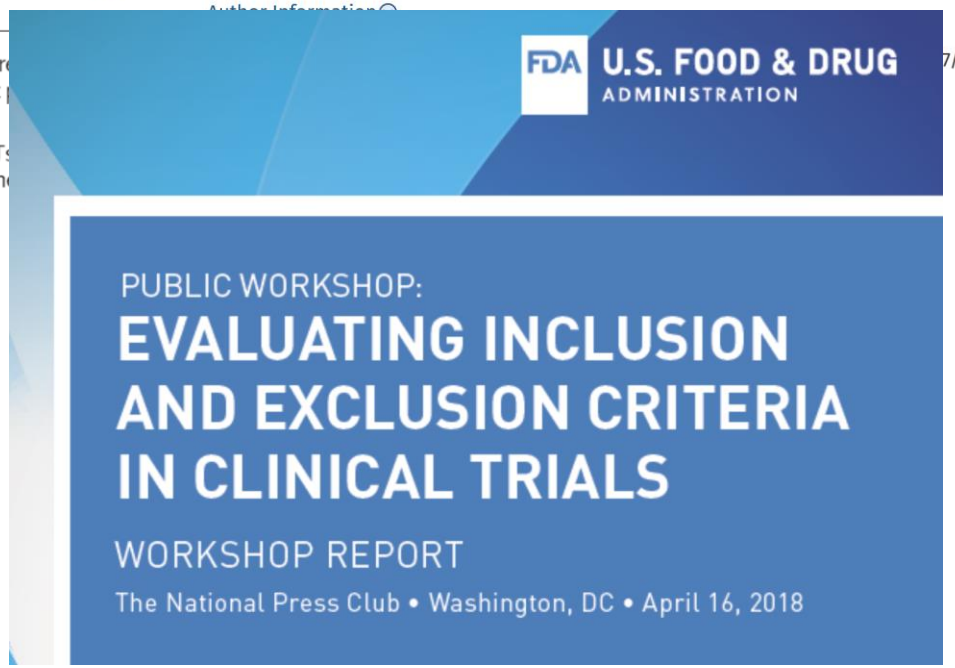
Explore content | About the journal | Publish with us | Subscribe

nature › news › article

NEWS | 03 April 2018

Cancer researchers push to relax rules for clinical trials

US government examines whether criteria for participating in drug studies unnecessarily exclude some people.



New ways of approaching inclusion/exclusion criteria

When designing clinical trials, there is tension between balancing the desire to minimize heterogeneity ("noise"), which can mask a finding of the effect, and the desire to generate data that are generalizable to a broader patient population that is likely to be treated.

There may be longstanding eligibility criteria practices that unnecessarily limit eligibility for certain patient populations. In designing eligibility criteria, sponsors, investigators, and regulators should avoid assumptions and revise criteria lacking clear scientific justification. . . . To reduce carryover effects from poorly-established eligibility criteria in previous trials, sponsors should spend additional time and resources ensuring that eligibility criteria are scientifically justifiable in every individual study.

FDA

Fogel DB. Factors associated with clinical trials that fail and opportunities for improving the likelihood of success: A review. Contemp Clin Trials Commun. 2018 Aug 7;11:156-164. doi: 10.1016/j.conctc.2018.08.001. PMID: 30112460; PMCID: PMC6092479.

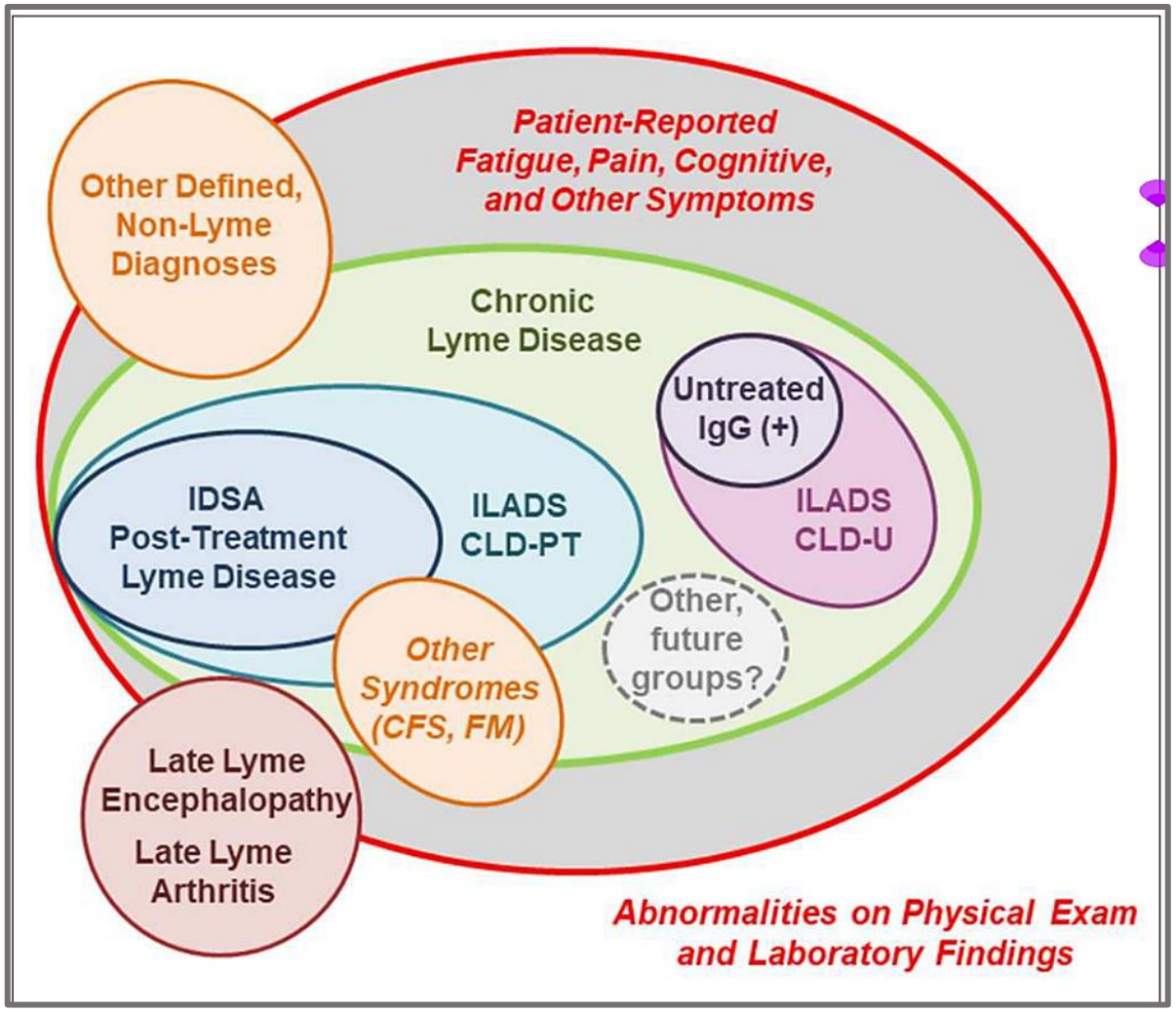
FDA, PUBLIC WORKSHOP: EVALUATING INCLUSION AND EXCLUSION CRITERIA IN CLINICAL TRIALS WORKSHOP REPORT
The National Press Club, Washington, DC . April 16, 2018

Definitions of persistent or chronic Lyme disease vary

Those who have persistent or chronic Lyme disease--diagnosed or not

ILADS (Clinical diagnosis): Patients who have been diagnosed with persistent Lyme disease

IDSA (RCT type research): Patients who have persistent Lyme disease for ≥ 6 months after treatment and who meet ≥40 other exclusionary criteria of the IDSA research definition of Post-Treatment Lyme Disease



Rebman 2020.

https://www.cdc.gov/me-cfs/healthcare-providers/case-definitions-criteria.html

Feasibility study on effect of inclusion/exclusion criteria

Who do we exclude and WHY (avoid exclusion creep and provide justification)

- What effect does the definition have on
  - Recruitment yield
  - Time to recruit
  - Cost to recruit
  - Maximizing statistical power
  - Generalizability of the findings to the clinical population
  - As well as the ability to determine cause and effect

Use Real World Evidence from patient registry can be used to conduct a trial run of inclusion/exclusion criteria before finalizing to determine the individual and cumulative effects of exclusion criteria selected

Visit us at www.LymeDisease.org

Enroll in MyLymeData at www.MyLymeData.org

Contact me at lorrainejohnson@outlook.com

Follow me on twitter @lymepolicywonk

References

Centers for Disease Control, ME/CFS **Understanding History of Case Definitions and Criteria** https://www.cdc.gov/me-cfs/healthcare-providers/case-definitions-criteria.html

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**, 10.1212/01.WNL.0000284604.61160.2d, 992-1003, doi:10.1212/01.WNL.0000284604.61160.2d http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=17928580

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, April 2014.

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, http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=12821734

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. *The New England journal of medicine* **2001**, 85-92, http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&dopt=Citation&list_uids=11450676

Rebman, A.W.; Aucott, J.N. Post-treatment Lyme Disease as a Model for Persistent Symptoms in Lyme Disease. *Front Med (Lausanne)* **2020**, *7*, 57, doi:10.3389/fmed.2020.00057 https://www.ncbi.nlm.nih.gov/pubmed/32161761 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7052487/pdf/fmed-07-00057.pdf.