

# Generalizability in two clinical trials of Lyme disease

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## Abstract

### Objective

To examine the generalizability of two National Institutes of Health (NIH)-funded double-blind randomized placebo-controlled clinical trials in patients with chronic Lyme disease and to determine whether selection factors resulted in the unfavorable outcomes.

### Design

Epidemiologic review of the generalizability of two trials conducted by Klempner et al. This paper considers whether the study group was representative of the general chronic Lyme disease population.

### Results

In their article in *The New England Journal of Medicine*, Klempner et al. failed to discuss the limitations of their clinical trials. This epidemiologic review argues that their results are not generalizable to the overall Lyme disease population. The treatment failure reported by the authors may be the result of enrolling patients who remained ill after an average of 4.7 years and an average of 3 previous courses of treatment. The poor outcome cited in these trials may be explained by having selected patients who had undergone delayed treatment or multiple treatments unsuccessfully. These selection factors were not addressed by the studies' authors, nor have they been discussed by reviewers. The trials have been over-interpreted by the NIH and widely publicized in a press release. The results have been extrapolated to other groups of Lyme disease patients by commentators, by a case discussant in an influential medical journal, and by health insurance companies to deny antibiotic treatment.

### Conclusion

The Klempner et al. trials are assumed to be internally valid based on a Randomized Control Trial (RCT) design. However, this review argues that the trials have limited generalizability beyond the select group of patients with characteristics like those in the trial. Applying the findings to target populations with characteristics that differ from those included in these trials is inappropriate and may limit options for chronic Lyme disease patients who might benefit from antibiotic treatment.