

# Rules of Treatment Discovery

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1. Medical outcomes in complex diseases are non-binary and heteroscedastic\*.
2. Every patient with a chronic illness has 5-20 symptoms that can be targeted as an outcome.
3. Some symptoms are “root” or “core” and shared by all other patients with the same disease. Other symptoms are “personalized” and are present in fewer than 20% of patients.
4. Symptomatic treatments directly target a given symptom but fail to collapse heteroscedasticity across all symptoms.
5. Root treatments are directed at a level that underlies and controls the dynamics of the causal network, but this target may not be recognized as a physical symptom. “The control panel can be separate from the engine.”
6. Root treatments collapse heteroscedasticity across symptoms and reveal a hidden correlation between core symptoms. In other words, root treatments act like a rising tide that floats all boats. When the network dynamics are restored, health is restored.
7. All drugs have side effects.
8. Side effects are non-binary and heteroscedastic.....
9. The math of non-binary outcomes and drug side-effects in chronic illness cannot be solved with N of 1 studies.
10. Reliable progress toward treatment discovery in complex diseases requires testing in a prospectively randomized, double-blind, placebo-controlled clinical trial. The size of early clinical trials can be scaled between N=10 to N=100 to meet financial and scientific goals.

\*Heteroscedastic is a statistical term that refers to the fact that when you measure the severity of a symptom using a numerical clinical scale (as for fatigue, pain, brain fog, GI symptoms, POTS, etc. in ME/CFS) the magnitude of the change in response to the same treatment varies across patients. Variances also change when you look at different treatments over time in the same patient. This has the effect of creating an unreliable estimate of the fraction of variance explained by any single drug when just one patient is evaluated, or even a handful of patients.