Comparing Classic Crossover Trials and Aggregated N-of-1 Trials: A Methodological White Paper

Abstract

Classic crossover trials and aggregated N-of-1 trials share surface similarities, including repeated administration of treatments within individuals and frequent use of mixed-effects models. However, despite this overlap, the designs differ fundamentally in structure, inferential goals, estimands, replication, and statistical modeling. This white paper elaborates on these differences and provides a PTSD example.

1 Introduction

Repeated-treatment clinical trial designs reduce between-person variability by allowing each participant to serve as their own control (**?**). N-of-1 trials extend this by providing dense repeated observations per participant (**??**). Despite surface similarities, the inferential goals and statistical structures differ (**?**).