

## **Small Sample, Sequential, Multiple Assignment, Randomized Trial (snSMART) Designs and Methods for Chronic, Rare Disease Drug Development**

**Instructor:** Kelley Kidwell, University of Michigan

**Course Description:** Sequential, multiple assignment, randomized trial (SMART) designs are often motivated to identify tailored sequences of treatments or dynamic treatment regimens (DTRs) in larger samples. SMARTs employ at least two randomizations in sequence where only some groups may be re-randomized based on response or other characteristics related to previous treatment. We have turned standard SMART designs and analyses on their head, and instead of focusing on DTRs, we apply the design to small samples to obtain more information from a small sample of individuals. This short course will provide an overview of small sample SMART (snSMART) designs with corresponding Bayesian and frequentist methods for analyses. The differences between snSMART and SMART designs will be highlighted and methods to analyze snSMART data, calculate sample size, add adaptive components, incorporate external data, and dose-find and confirm will be presented. Many of our methods are motivated by the current snSMART ARAMIS which seeks to find an effective treatment for individuals with isolated skin vasculitis, but the methods apply broadly to chronic, rare diseases that remain relatively stable over the trial period.