Lab 02 - R Essentials

Learning goals

Today's lab is the first steps toward designing a response-adaptive randomization (RAR) trial. RAR designs are used in precision medicine trials, such as the BATTLE trial, to gather early evidence of treatment arms that work best for a given biomarker. Throughout RAR, the treatment allocation adjusts depending on which treatment arm looks most promising. We will focus on the initial steps of coding this design.

The lab is motivated by the paper by Kurt Viele: Comparison of methods for control allocation in multiple arm studies using response adaptive randomization. It practices:

- Pre-allocating vectors
- Using a loop
- Writing a function

Notation

Notation and criteria for study to successfully declare a treatment as efficacious:

- $i = 1, \ldots, N$ participants
- $t = 0, 1, 2, 3$ study arms ($t = 0$ is control)
- $Y_i \mid t \sim$ Bern(p_t) and y_t is a vector of n_t observed outcomes on arm t
- The prior on $p_t \sim$ Beta(α_t, β_t)

Posterior Distribution Pr($p_t \mid y_t$) $\sim$ Beta($\alpha_t + \sum y_t, \beta_t + n_t - \sum y_t$)

Quoting from the paper: The trial is considered successful at the final analysis if there is a high posterior probability that at least one arm has a higher rate than control.

$\max_t$ Pr($p_t > p_0$) > δ

where δ is a threshold chosen to maintain familywise type I error for the study at one-sided 2.5%.

Consider 2 different designs:

1. Equal allocation to four arms throughout design.
2. RAR where the allocation probability is updated at an interim analysis as follows:

- $V_t = P_t$ (Max)
- $V_0 = min\{\sum V_t \frac{(n_t+1)}{(n_0+1)}, max(V_1, V_2, V_3)\}$

V_0, V_1, V_2, and V_3 are renormalized to sum to 1 and are allocation probabilities.

Note: A way to estimate P_t(Max) is to `cbind` K = [1000] draws from the posterior distribution of each arm and to see how frequently (across the K draws from each arm) each arm is drawn to be the largest.

Lab task:

Write a function for each study design to simulate one trial.

- N = 228 with interim analyses after every 40th participant starting at 40.
- Use equal allocation for first 40 patients for both designs.
- Assume a setting where treatment effect is 0.35 for each study arm (the null scenario). (But allow flexibility in function for other treatment effects).
- $\alpha_t = 0.35$ for all t and $\beta_t = 0.65$ for all arms.
- Use the following δ thresholds to determine a successful trial:
  - Design 1, $\delta = 0.9912$
  - Design 2, $\delta = 0.9892$

For simplicity, have your function return a list of at least the following output:

1. The probability that the best treatment arm is better than control.
2. The number of patients assigned to each treatment arm.

If you have more time

- Replicate the design many (10K) times. Calculate the Type I error.
- Find δ for each design (supposing you didn't already know it).
- Replicate the study design assuming treatment effects of
  - $p_0 = p_1 = p_2 = 0.35$
  - $p_3 = 0.65$