Upstrapping to Determine Futility & Efficacy in Interim Monitoring (outline)

1. Introduction/Background
   1. TREATNOW trial context/motivation
   2. Interim monitoring background
      1. GSD
      2. Upstrapping
2. Methods
   1. Upstrapping algorithm description
   2. Simulations
      1. Simulation setting criteria
      2. Data simulation process
      3. Modeling strategy
   3. Upstrapping method validation
      1. Heatmap generation from simulations
   4. Calibration
      1. Different calibration strategies
         1. Arbitrary
         2. Strictly fixed p value variable proportion
         3. Fixed p value variable proportion
         4. Strictly fixed proportion variable p value
         5. Fixed proportion variable p value
         6. Variable p value and proportion
   5. Upstrapping application to simulated data
      1. Arbitrary upstrapping thresholds
      2. Calibrated upstrapping thresholds
      3. Alpha/beta spending functions
      4. GSD
3. Results
   1. Upstrapping method validation results
      1. Heatmap results
      2. Interpretation
   2. Calibration results
      1. Selected calibration thresholds
      2. Calibration recommendations
   3. Upstrapping application results
      1. Likelihood to stop for futility/efficacy
         1. Compare between methods
         2. Compare between simulation settings
4. Discussion
   1. Limitations
      1. Sample size/interim stopping point considerations
      2. Simplified simulation settings (see next paper)
      3. Calibration considerations
         1. Power and type I error trade off – potential to define novel spending function
   2. Conclusions
      1. Upstrapping is/is not a valid method (or only valid in limited circumstances/with tradeoffs)