SEPSIS

Additional Simulations

2020-10-16

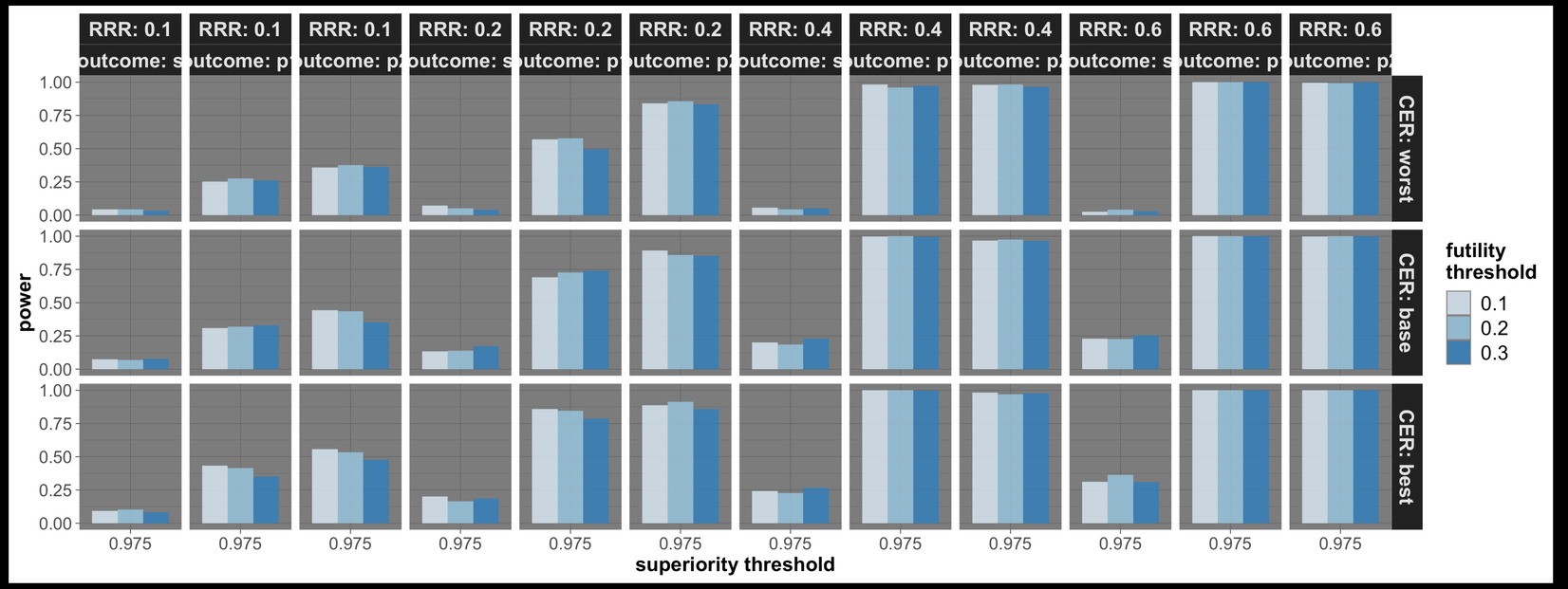
Additional Simulations

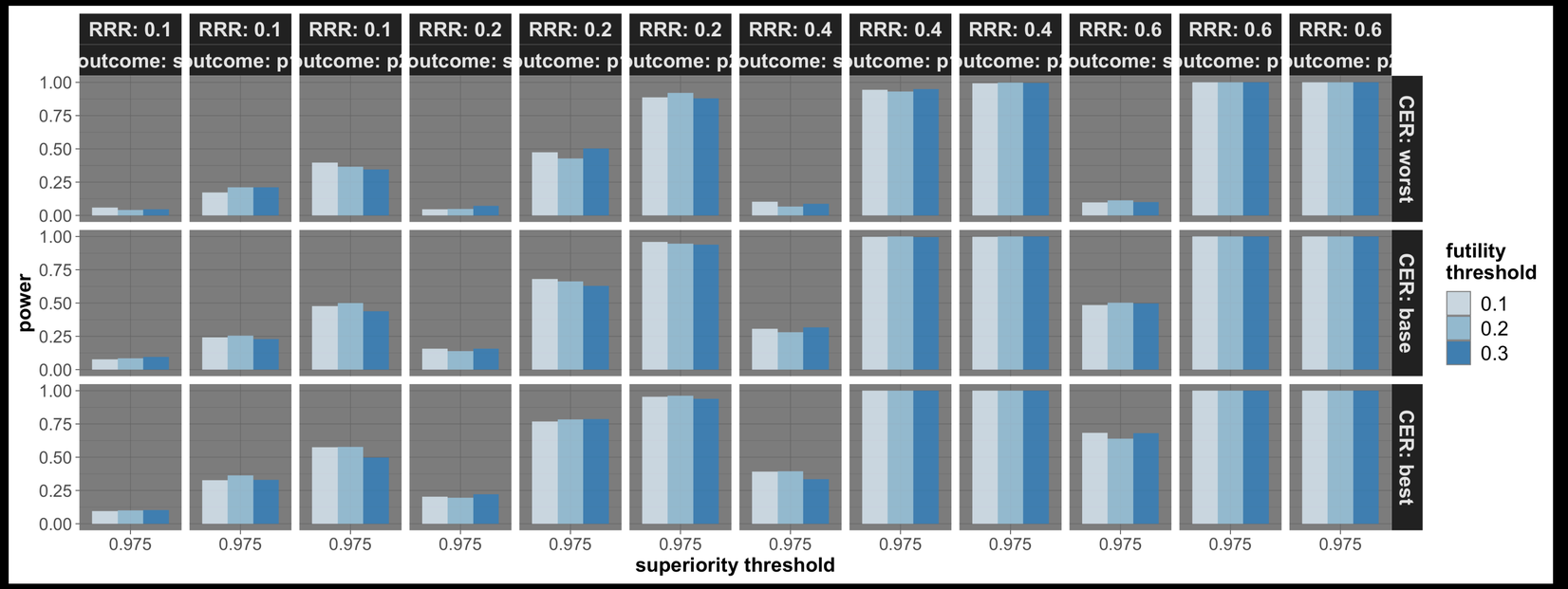
- Stopping for both superiority and futility w.r.t moderately permissive outcome (p1)
- Superiority and futility thresholds held fixed at 0.975 and 0.99, respectively
- Added an additional Relative Risk Reduction (RRR) of 0.1
- Investigated variable number of interim analyses (batch size of 1k, 2k, and 3k)
  - Note: since the number of patients at the end of the trial is random, the number of interim analyses is also random
  - This number is controlled through “batch size”, which is the number of enrolled patients being enrolled before a look at the data occurs
  - E.g. If the number of patients at the end of the trial is 6,000 and analyses occurred every 1,000 patients, there would be six analyses completed

Power

Batch size: 1,000 (top) vs 3,000 (bottom)

- Moderate to high power for p1 and p2 for both more frequent (top) and less frequent (bottom) interim analyses when RRR >= 0.2
- Low power for s
- In general, improves as CER improves



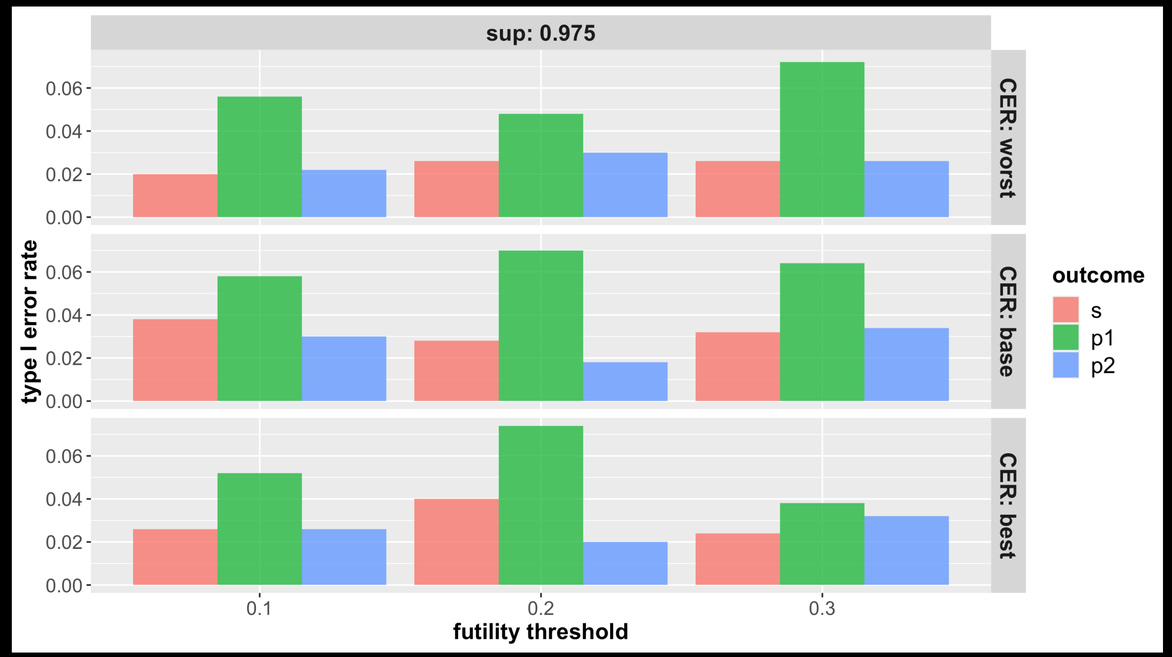


False Positive Rate

Batch size: 1,000 (top) vs 3,000 (bottom)

- False positive rate for p1 higher since repeated testing is happening on this outcome

- For more frequent interim analyses (top), false positive rate is higher (~10% for p1)



Expected Sample Size

Batch size: 1,000 (top) vs 3,000 (bottom)

- As true relative risk reduction increases and CER improves, expected sample size decreases
- With fewer interim analyses (bottom), expected sample size increases