Adaptive Methods in Clinical Research

Practical 2 Solutions: Group Sequential Designs

Q1

```
> power.t.test(delta = 0.5, type = "two.sample", alternative = "one.sided"
, power = 0.9)

     Two-sample t test power calculation

              n = 69.19782
          delta = 0.5
             sd = 1
      sig.level = 0.05
          power = 0.9
    alternative = one.sided

NOTE: n is number in *each* group
```

Q3: Two-stage O'Brien-Fleming stopping boundaries

a) Maximum sample size = 138.971
b) ESS under the null = 137.745
c) ESS under the alternative = 112.13
d) P(stop for lack of benefit at stage 1 under the null) = 0.009
e) P(stop for efficacy at stage 1 under the alternative) = 0.386

Single stage (fixed sample) design has sample size = 138.40

Q4: Two-stage Pocock stopping boundaries

a) Maximum sample size = 152.022
b) ESS under the null = 147.412
c) ESS under the alternative = 104.934
d) P(stop for lack of benefit at stage 1 under the null) = 0.03
e) P(stop for efficacy at stage 1 under the alternative) = 0.62

Q5

ESS for null-optimal design under the null = 95.579

ESS for alternative-optimal design under the alternative = 104.447

Q6

O'Brien-Fleming stopping boundaries

No. of stages	Maximum sample size	ESS under the null	ESS under the alternative
2	139.0	137.7	112.1
3	140.4	138.5	106.0
4	141.1	139.1	102.1
5	142.1	139.5	99.7

Pocock stopping boundaries

No. of stages	Maximum sample size	ESS under the null	ESS under the alternative
2	152.0	147.4	104.9
3	159.7	153.1	96.8
4	164.7	156.9	93.3
5	168.3	159.7	91.5

Maximum sample size increases, ESS under the null increases, ESS under the alternative decreases

Diminishing differences as number of stages increases

Q7

O'Brien Fleming stopping boundaries

Maximum sample size = 156.34

ESS under the null = 154.96

ESS under the alternative = 126.15

Pocock stopping boundaries

Maximum sample size = 171.03

ESS under the null = 165.84

ESS under the alternative = 118.05

Larger maximum sample size and ESS *but* many more patients given the experimental treatment relative to the control.

This may be a preferred approach if there is a strong ethical (patient benefit) rationale to give experimental treatment.