*Stat 622/422 (Dr. Baron) Advanced Biostatistics*

**Group sequential clinical trials**

**# Design a Pocock group sequential clinical trial with**

**# five equal groups, distance 2.9 between the null and**

**# alternative parameters, standard deviation 4.8,**

**# significance level 0.05, and power 0.9.**

> library(clinfun)

> gsdesign.normal( ifrac=(1:5)/5, delta=2.9, sd=4.8,

+ sig.level=0.05, power=0.9, delta.eb=0)

Group sequential design for comparing normal data with delta = 2.9 , sd = 4.8

power family of boundary; 0 (Pocock) to 0.5 (O'Brien-Fleming)

sample size (per arm) = 69.52065

information fraction = 0.2 0.4 0.6 0.8 1.0

efficacy boundary = 2.414 2.414 2.414 2.414 2.414 (power = 0)

sig.level = 0.05

power = 0.9

alternative = two.sided

**# Here ifrac = information fraction (0.2, 0.4, ..., 1.0),**

**# delta.eb = boundary for efficacy, it = 0 means Pocock boundaries**

**# (delta.fb = boundary for futility, = 0.5 means O'Brien-Fleming)**

**# As a result, we sample ceiling(69.6/5) = 14 patients for each group.**

**# The trial will stop and reject Ho as soon as |Z(k)| > 2.417.**

**# Design an O'Brien-Fleming test for the same problem.**

> gsdesign.normal( ifrac=(1:5)/5, delta=2.9, sd=4.8,

+ sig.level=0.05, power=0.9, delta.eb=0.5)

Group sequential design for comparing normal data with delta = 2.9 , sd = 4.8

power family of boundary; 0 (Pocock) to 0.5 (O'Brien-Fleming)

sample size (per arm) = 59.13287

information fraction = 0.2 0.4 0.6 0.8 1.0

efficacy boundary = 4.564 3.227 2.635 2.282 2.041 (power = 0.5)

sig.level = 0.05

power = 0.9

alternative = two.sided

**> # For the O'Brien-Fleming test, we sample ceiling(59.1/5) = 12 patients**

**> # for each group. The trial will stop**

**> # - after the 1st group if |Z(1)| > 4.56, otherwise,**

**> # - after the 2nd group if |Z(2)| > 3.224, otherwise,**

**> # - after the 3rd group if |Z(3)| > 2.633, otherwise,**

**> # - after the 4th group if |Z(4)| > 2.28, otherwise,**

**> # - after the 5th group if |Z(5)| > 2.039.**