

Module 5 - Design and Monitoring of Group Sequential Trials
University of Washington - Summer Institute in Biostatistics

Session 5 In-Class Problems

1. Monitoring the sepsis trial: In this problem we will consider monitoring the sepsis trial using constrained boundaries as implemented in `seqMonitor()`.

- (a) Start by specifying the following design that was originally considered by the study sponsor:

```
##
##### Definition of sponsor's chosen stopping rule
##
binomFixed <- seqDesign( prob.model = "proportions", arms = 2, null.hypothesis = .3,
alt.hypothesis = 0.25, ratio = c(1., 1.), nbr.analyses = 1,
test.type = "less", power = 0.80, alpha = 0.025 )
binomFixed.1700 <- update( binomFixed, sample.size=1700, power="calculate" )

bnd <- rbind( c(1-.0001, NA ),
rep(NA,2), rep(NA,2),
rep(NA,2), rep(NA,2) )
bnd <- seqBoundary( bnd, scale="P" )

sepsis.Sponsor <- update( binomFixed.1700, nbr.analyses=5, P=c(1,.75) )
sepsis.Sponsor <- update( sepsis.Sponsor, exact.constraint=bnd )
```

- (b) Now, download the hypothetical data observed at the time of the first interim analysis using the following command:

```
interim1 <- read.csv( "http://rctdesign.org/ShortCourses/uwAugust2013/interim1Data.csv",
header=TRUE )
```

In this data file, `tx1` is the treatment indicator for each group (1=antibody, 0=placebo) and `resp1` indicates whether the patient died within 28 days. Using these data, implement the first interim analysis using `seqMonitor()` where the maximal sample size is adjusted to maintain power. Plot the result and discuss the conclusions from the first analysis.

- (c) Now, download the hypothetical data observed at the time of the second interim analysis using the following command:

```
interim2 <- read.csv( "http://rctdesign.org/ShortCourses/uwAugust2013/interim2Data.csv",
header=TRUE )
```

In this data file, `tx2` is the treatment indicator for each group (1=antibody, 0=placebo) and `resp2` indicates whether the patient died within 28 days. Using these data, implement the second interim analysis using `seqMonitor()` where the maximal sample size is adjusted to maintain power and boundaries are constrained to those implemented at the first analysis. Plot the result and discuss the conclusions from the second analysis.