

# Homework 2

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```
# load the needed packages
library(tidyverse)
knitr::opts_chunk$set(echo = TRUE)
options(digits = 3)
```

## Problem one

Suppose we are comparing a new treatment to standard-of-care. We run a randomized clinical trial (with basic simple randomization), and would like to assess if treatment is more effective than control (using a binary outcome — response vs non-response). Suppose efficacy is assessed by the difference in response proportion between new-treatment and standard-of-care. Please write a function that takes in data from a clinical trial run as above (a matrix with two columns: tx for treatment assignment, and outcome, with outcome=1 indicating response), and runs a permutation/re-randomization test to evaluate if the data are consistent with the hypothesis that standard-of-care is at least as effective as new-treatment.

For this question, the statement is that the treatment group is no more effective than the control group. Next, we use the response proportion as the measure. And then we do the simulation under the statement. Finally, we compare the measure evaluated on that simulated data to the measure on the original data.

```
# The first column named tx, tx=1 indicating the treatment group.
# The second column named outcome.

### Let's evaluate things via permutation ###
simulate.perm.trial <- function(data){
  ## create the permuted data ##
  perm <- sample(1:nrow(data), replace = FALSE)
  perm.data <- data
  perm.data$tx <- data$tx[perm]

  ## calculate the response proportion differences on permuted data
  prop.per.arm <- perm.data %>% group_by(tx) %>% summarise(prop=mean(outcome))
  # use treatment minus control
  perm.prop.diff <- prop.per.arm[2,2]-prop.per.arm[1,2]
  return(perm.prop.diff$prop)
}

### write the function that can do many times simulation and evaluate if the data are consistent with t.

all <- function(data,nsim){

  #Getting numerical summary of response proportion of the original data
  prop.summ <- data %>%
    group_by(tx) %>%
```

```

        summarise(prop=mean(outcome))
diff.summ <- prop.summ[2,2] - prop.summ[1,2]

### Running a large number of simulated trials for the response proportion ###
permuted.stats <- data.frame(replicate(nsim, simulate.perm.trial(data)))
colnames(permuted.stats) <- c("prop.diff")

# Compute the density data
dens <- density(permuted.stats$prop.diff)
# plot density
plot(dens, frame = FALSE, col = "steelblue",
     main = "density plot of the response proportion difference")
abline(v=diff.summ$prop)

# Calculating tail probabilities
tail <- 1-mean(permuted.stats$prop.diff <= diff.summ$prop)
return(tail)
}

```

## Problem two

2a) Please write a function that will take in data from a trial run as above (ie. a matrix with one column tx of treatment assignments, one column outcome of binary outcomes, and one column order of enrollment order) and run a rerandomization test. The test should assess if the observed difference in response proportions is consistent with the hypothesis that standard-of-care is at least as effective as the new-treatment.

```

### Let's evaluate things via single permutation through adaptive design###
simulate.trial.adap <- function(data){
  # success in treatment plus failure in control is equal to k
  # initialize k= 0 in the first patient
  k <- 0
  # each row/patient has different probability in the binomial experiment
  for (i in (1:nrow(data))) {
    p <- (1+3*k)/(2+3*(data$order[i]-1))
    # tx.perm is the result of the assignment (treatment or control)
    data$tx.perm[i] <- rbinom(1,1,p)
    if (data$tx.perm[i]==data$outcome[i]) {
      k <- k+1
    }
  }
}

prop.summ <- data %>%
  group_by(tx.perm) %>%
  summarise(prop=mean(outcome))
diff.summ <- prop.summ[2,2] - prop.summ[1,2]
return(diff.summ$prop)

}

all2 <- function(data,nsim){
  #Getting numerical summary of response proportion of the original data
  prop.summ <- data %>%
    group_by(tx) %>%

```

```

      summarise(prop=mean(outcome))
diff.summ <- prop.summ[2,2] - prop.summ[1,2]

  ### Running a large number of simulated trials for the response proportion ###
  permuted.stats <- data.frame(replicate(nsim, simulate.trial.adap(data)))
  colnames(permuted.stats) <- c("prop.diff")

  # Compute the density data
  dens <- density(permuted.stats$prop.diff)
  # plot density
  plot(dens, frame = FALSE, col = "steelblue",
       main = "density plot of the response proportion difference (adaptive)")
  abline(v=diff.summ$prop)

  # Calculating tail probabilities
  tail <- 1-mean(permuted.stats$prop.diff <= diff.summ$prop)
  return(tail)
}

```

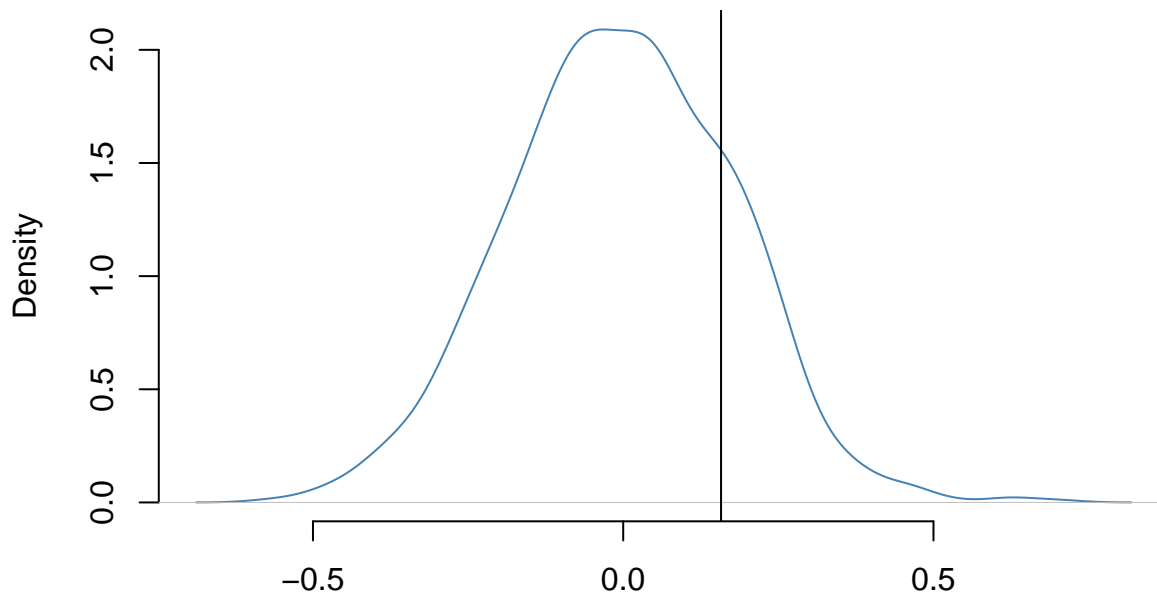
2b) Please read in the data “HW2-adaptive-trial.txt” from the website; and, using your function from (2a), evaluate if the data are consistent with the hypothesis that standard-of-care is at least as effective as the new treatment.

```

# read the data for later use
data <- read.table("/Users/ziyuxiao/Desktop/UW/Fall2020/BIOST544/data/HW2-adaptive-trial.txt", sep = ",",
set.seed(3)
nsim <- 1000
all2(data,nsim)

```

### **density plot of the response proportion difference (adaptive)**



```
## [1] 0.207
```

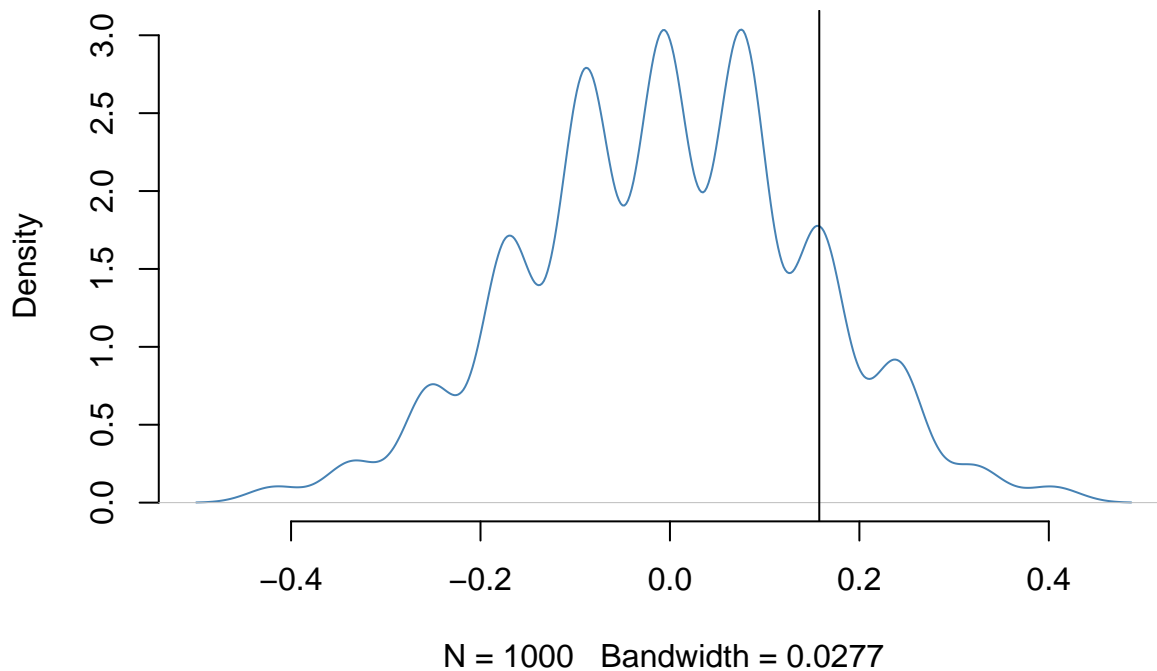
Since  $p=0.207>0.05$ , we fail to reject the null hypothesis that standard-of-care is at least as effective as the new treatment.

## Problem three

Now suppose a collaborator provided the data in “HW2-adaptive-trial.txt”, but forgot to say that they were generated using an adaptive trial. In this case we would likely accidentally analyze our data using the function written in (1). How does the sampling distribution of the response difference generated from new old the simple permutations in (1) compare to the sampling distribution generated using our adaptive rerandomization from the function in (2a)?

```
set.seed(3)
nsim <- 1000
all(data,nsim)
```

### density plot of the response proportion difference



```
## [1] 0.085
```

Since  $p=0.085>0.05$ , we fail to reject the null hypothesis that standard-of-care is at least as effective as the new treatment.

The final result is the same that both of them fail to reject the null hypothesis. However, the p-value is quite different. Besides the sample distribution is more wiggly by using the simple permutation in problem 1 than the one using adaptive rerandomization. We are more likely to fail to reject the null hypothesis by using the adaptive rerandomization.