office hours
Tues: 4-5

STA305/1004 - Class 5

September 19, 2019

Today's Class

- Paired Comparisons
- Introduction to Phase III Clinical Trials
- Introduction to power

Paired Comparisons

- Increase precision by making comparisons within matched pairs of experimental material.
- Randomize within a pair.

Boy's Shoe Experiment

- Two materials to make boy's shoes, A and B, are tested to evaluate if B is more sturdy compared to A.
- During the experimental test some boys scuffed their shoes more than others.
- Each boy's two shoes were subjected to the same treatment by having each boy wear both materials.
- Working with 10 differences B-A most of the boy-to-boy variation could be eliminated.
- Called a randomized paired comparison design.

Boy's Shoe Experiment

- Toss a coin to randomize material to L/R foot of a boy.
- Head: Material A used on right foot.
- Null hypothesis: amount of wear associated with material A and B are the same.
- So labelling given to a pair of results only affects the sign of the difference.

H_0

Boy	Mat A		MAT B	diff	Could have been.
1	L	x	R	y	$x-y$.	$-(x-y)$

Randomized paired comparison

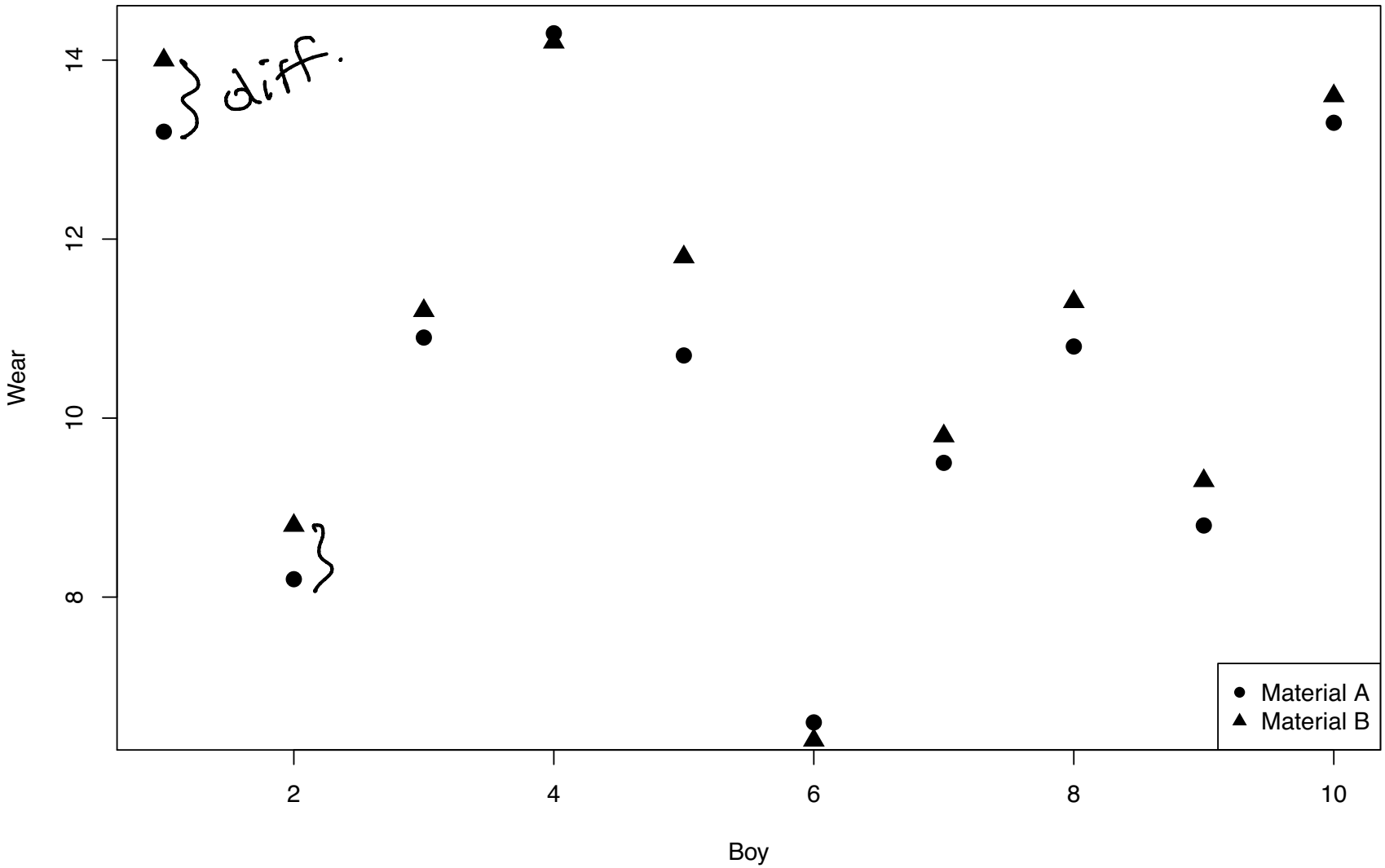
```
library(BHH2)
data(shoes.data)
shoes.data
```

load data into env.

```
##    boy matA sideA matB sideB
## 1    1 13.2     L 14.0     R
## 2    2  8.2     L  8.8     R
## 3    3 10.9     R 11.2     L
## 4    4 14.3     L 14.2     R
## 5    5 10.7     R 11.8     L
## 6    6  6.6     L  6.4     R
## 7    7  9.5     L  9.8     R
## 8    8 10.8     L 11.3     R
## 9    9  8.8     R  9.3     L
## 10  10 13.3     L 13.6     R
```

Randomized paired comparison

```
plot(shoes.data$boy,shoes.data$matA,pch=16,cex=1.5,
     xlab="Boy",ylab="Wear")
points(shoes.data$boy,shoes.data$matB,pch=17,cex=1.5)
legend("bottomright",legend=c("Material A","Material B"),pch=c(16,17))
```



Randomized paired comparison

```
diff <- shoes.data$matA-shoes.data$matB
meandiff <- mean(diff); meandiff
```

```
## [1] -0.41
```

```
shoe.dat2 <- data.frame(shoes.data,diff)
shoe.dat2[1:3,]
```

```
##   boy matA sideA matB sideB diff
## 1   1 13.2     L 14.0     R -0.8
## 2   2  8.2     L  8.8     R -0.6
## 3   3 10.9     R 11.2     L -0.3
```

```
mean(shoe.dat2$matA) - mean(shoe.dat2$matB)
```

```
## [1] -0.41
```

```
sd(diff)
```

```
## [1] 0.3871549
```

```
sqrt(sd(shoe.dat2$matA)^2/length(shoe.dat2$matA) +
     sd(shoe.dat2$matB)^2/length(shoe.dat2$matB))
```

```
## [1] 1.111381
```

Calc. diff.

adding the variable diff. to Shoe data.

— printout first three rows and all Col cmns

Why Calc - paired diffs?

$$Var(\bar{X}_a - \bar{X}_b) = Var(\bar{X}_a) + Var(\bar{X}_b)$$

$$= \frac{\sigma_A^2}{n_a} + \frac{\sigma_B^2}{n_b}$$

> 0.387.

Reduced variation of diff-estimate.

Boy's Shoe Experiment

$2 \times 2 \times 2 \times \cdots \times 2 = 2^{10}$

boy 1 2 3 ... 10

why ??

- The sequence of coin tosses is one of $2^{10} = 1024$ equiprobable outcomes.
- To test H_0 the average difference of -0.41 observed observed can be compared with the other 1023 averages by calculating the average difference for each of 1024 arrangements of signs in:

$$\bar{d} = \frac{\pm 0.8 \pm 0.6 \cdots \pm 0.3}{10}$$

1024 diffs

Randomized paired comparison

```
N <- 2^(10) # number of treatment assignments
res <- numeric(N) #vector to store results
LR <- list(c(-1,1)) # difference is multiplied by -1 or 1
# generate all possible treatment assign
trtassign <- expand.grid(rep(LR, 10))

for (i in 1:N) {
res[i] <- mean(as.numeric(trtassign[i,])*diff)
}
trtassign[1:2,]
```

← first 2 treatment assignments.

```
##   Var1 Var2 Var3 Var4 Var5 Var6 Var7 Var8 Var9 Var10
## 1   -1   -1   -1   -1   -1   -1   -1   -1   -1    -1
## 2    1   -1   -1   -1   -1   -1   -1   -1   -1    -1
```

```
res[1:2]
```

```
## [1] 0.41 0.25
```

← print of first 2 diffs.

R Notation

`res` is a vector of length 2^{10}.

```
length(res)
```

```
## [1] 1024
```

- The i^{th} element of `res` can be accessed using the notation `res[i]`, and `res[-i]` will return all the elements of `res` except the i^{th} element.
- `trtassign` is a 1024×10 matrix.

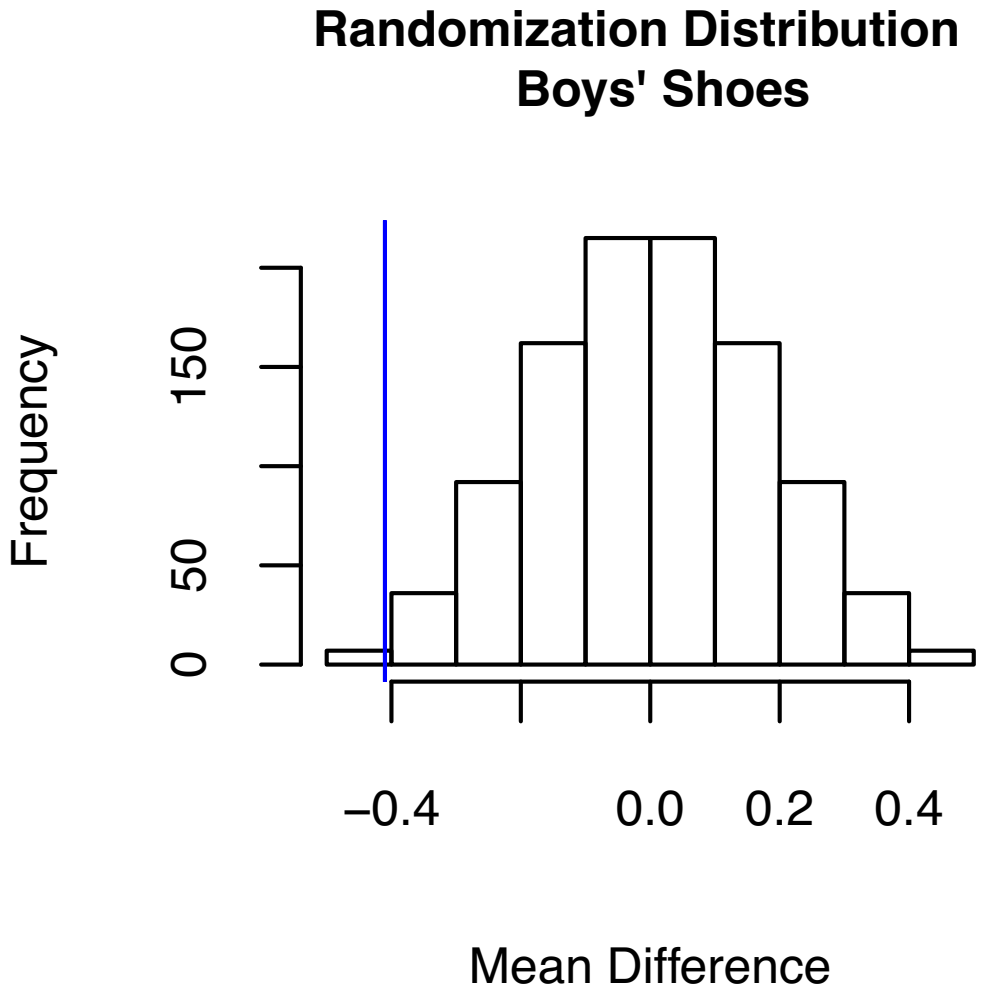
```
dim(trtassign)
```

```
## [1] 1024   10
```

- `trtassign[i,j]` will return the value of trtassign that is in the i^{th} and the j^{th} column.

Randomized paired comparison

```
hist(res, xlab = "Mean Difference",
     main = "Randomization Distribution  \n  Boys' Shoes",
     cex.main = 0.75, cex.lab = 0.75, cex.axis = 0.75)
abline(v = meandiff,col = "blue")
```



Randomized paired comparison

```r
# number of differences less than observed diff
sum(res <= meandiff)
```

```
## [1] 7
```

```r
# p-value
sum(res <= meandiff)/N
```

```
## [1] 0.006835938
```

R Notation

- `res <= meandiff` compares each element of `res` to `meandiff` and returns `TRUE` or `FALSE` which is *coerced* to a numeric via `TRUE` $\rightarrow$ 1 and `FALSE` $\rightarrow$ 0.
- `sum` counts the number of times elenments of the `res` vector are less than or equal to `meandiff`.

```
res[1:4] <= meandiff
```

```
## [1] FALSE FALSE FALSE FALSE
```

```
# explicit coercion to type numeric
as.numeric(res[1:4] <= meandiff)
```

```
## [1] 0 0 0 0
```

Paired t-test

$H_0: \mu_D = 0$ vs $H_a: \mu_D < 0$

If we assume that the differences -0.8, -0.6, -0.3, 0.1, -1.1, 0.2, -0.3, -0.5, -0.5, -0.3 are a random sample from a normal distribution then the statistic

$$t = \frac{\bar{d}}{s_{\bar{d}}/\sqrt{10}} \sim t_{10-1},$$

where, $s_{\bar{d}}$ is the sample standard deviation of the paired differences. The p-value for testing if $\bar{D} < 0$ is

$$P(t_9 < t).$$

Paired t-test

In general if there are n differences then

$$t = \frac{\bar{d}}{s_{\bar{d}}/\sqrt{n}} \sim t_{n-1},$$

where, $s_{\bar{d}}$ is the sample standard deviation of the paired differences. The p-value for testing if $\bar{D} < 0$ is

$$P(t_{n-1} < t).$$

NB: This is the same as a one-sample t-test of the differences.

Paired t-test

In R a paired t-test can be obtained by using the command `t.test()` with `paired=T`.

```
t.test(shoes.data$matA,shoes.data$matB,paired = TRUE,
       alternative = "less")
```

```
##
##  Paired t-test
##
## data:  shoes.data$matA and shoes.data$matB
## t = -3.3489, df = 9, p-value = 0.004269
## alternative hypothesis: true difference in means is less than 0
## 95 percent confidence interval:
##        -Inf -0.1855736
## sample estimates:
## mean of the differences
##                   -0.41
```

Ignore 95% CI in one-sided test.

Paired t-test

This is the same as a one-sample t-test on the difference.

```
# same as a one-sample t-test on the diff
t.test(diff,alternative = "less")
```

```
##
##  One Sample t-test
##
## data:  diff
## t = -3.3489, df = 9, p-value = 0.004269
## alternative hypothesis: true mean is less than 0
## 95 percent confidence interval:
##        -Inf -0.1855736
## sample estimates:
## mean of x
##     -0.41
```

Paired t-test

```
qqnorm(diff); qqline(diff)
```