Lab 12: Answers

April 10-11, 2018

Objectives

1. Discuss how to analyze studies that have two unmatched/unpaired groups with continuous outcomes
2. Practice calculating and interpreting a two sample t-test and confidence intervals
3. Discuss assumptions for two sample t-test and use the Welch's test

Infant Diarrhea Study

Diarrhea is a major public health problem in underdeveloped countries, especially for babies. Diarrhea leads to dehydration, which results in millions of deaths each year worldwide.

Researchers in Peru conducted a double-blind randomized controlled trial, published in The New England Journal of Medicine, to determine whether Bismuth salicylate would improve the outcomes of infants suffering from diarrhea.

In their study, all infants received the standard therapy for diarrhea: oral rehydration. In addition to the rehydration, 85 babies received bismuth salicylate, while 84 babies received a placebo. The total stool volumes for all infants over the course of their illness was measured. To adjust for body size, the researchers divided by body weight to obtain their outcome of interest: stool output per kilogram of body weight. The results of their study are available on the course website.

```
DiaData <- read.delim("http://myweb.uiowa.edu/pbreheny/data/diarrhea.txt")
```

Explore the data

Let's examine the distribution of stool output by group using a boxplot of the data:

```
boxplot(DiaData$Stool ~ DiaData$Group, col = rainbow(2), main = "Effect of bismuth salicylate")
```
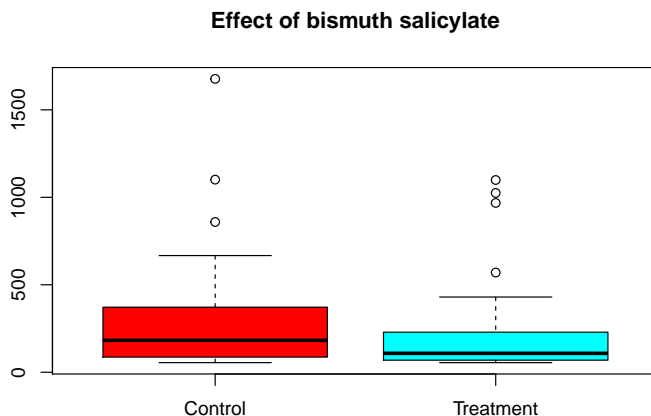

Summarize the distribution and describe any differences you notice about the two groups

1

Two Sample t-tests

Student's two sample t-test

To do a students two sample t-test we must be able to find the standard deviation using a pooled variance, standard error, and the t statistic. These three can be found using the equations below (which are also in your lecture slides:

Test statistic:

$SD_{(pooled)} = \sqrt{\frac{(n_1-1)S_1^2+(n_2-1)S_2^2}{n_1+n_2-2}}$

$SE_d = SD_{(pooled)}\sqrt{\frac{1}{n_1} + \frac{1}{n_2}}$

$t = \frac{\bar{x}_1-\bar{x}_2}{SE_d}$ with $n_1 + n_2 - 2$ degrees of freedom

$df = n_1 + n_2 - 2$

Confidence interval:

$\bar{x}_1 - \bar{x}_2 \pm t_{\alpha/2} * SE_d$

So as you can tell we need to compute several statistics from the data in order to do this t-test. We need to compute the mean of continuous outcomes for both groups and those will be out $\bar{x}_1$ and $\bar{x}_2$ as well as the standard error above.

What is our null hypothesis for this data?

Calculate the test statistic and 95% confidence interval by hand. Summarize your results.

As a reminder, here are some helpful functions for finding summary statistics:

```
#Find n in each group
table(DiaData$Group)

#Find mean of each group
by(DiaData$Stool, DiaData$Group, mean)

#Find standard deviation of each group
by(DiaData$Stool, DiaData$Group, sd)
```

Check with R

Comments about t.test code:

Notice you use the tilde (~) to specify that you want to look at stool output by group. You use the tilde because all stool outputs are in one column and group is given in another column. If you were given the stool outputs in two columns (Control & Treatment), then you would simply give R the two columns separated by a comma. It would look something like: t.test(Treatment, Control, var.equal = TRUE). See last lab 10 'Anorexia' data for an example of data for each group given by column.

We no longer have to say paired=TRUE. The default is paired=FALSE and that is exactly the test we want.

We have to specify that we are assuming the variance is equal using the argument var.equal=TRUE, otherwise the results will **not** be the same as the results we computed by hand.

```
t.test(DiaData$Stool~DiaData$Group, var.equal = TRUE)
```

Welch's two sample t-test

When we calculated the two sample t-test by hand, we had to assume the variance (square of the standard deviation) was equal.

Review the standard deviations of the two groups and describe whether you think the assumption is met

If the variances were not similar, we would consider using the Welch's two sample t-test. The Welch's test accounts for data that do not have equal variances, providing us with a more accurate test result if the assumption of equal variances is violated. To do this test by hand is quite computational so we will learn how to compute it in R.

To conduct a Welch's test, we simply switch the variance argument to var.equal= FALSE. This is also the default, so you can leave out the argument entirely and get the same answer.

```r
t.test(DiaData$Stool~DiaData$Group, var.equal = FALSE)
```

Here our p-value is very close to the one we obtained using the Student's test. This will generally be the case when the variances are so close.

Practice Problems: Heart Study

Some infants are born with congenital heart defects and require surgery very early in life. One approach to performing this surgery is known as "circulatory arrest." A downside of this procedure, however, is that it cuts off the flow of blood to the brain, possibly resulting in brain damage. An alternative procedure, "low-flow bypass" maintains circulation to the brain, but does so with an external pump that potentially causes other sorts of injuries to the brain.

To investigate the treatments, surgeons at Harvard Medical School conducted a randomized controlled trial. In the trial, 70 infants received low-flow bypass surgery and 73 received the circulatory arrest approach. The researchers looked at two outcomes: the Psychomotor Development Index (PDI), which measures physiological development, and the Mental Development Index (MDI), which measures mental development. For both indices, higher scores indicate greater levels of development. The results of their study are on the course website.

Use:

```r
heart <- read.delim("http://myweb.uiowa.edu/pbreheny/data/infant-heart.txt")
```

a) Calculate the standard deviations of PDI and MDI for each group. Based on these values, should we do a Student's test or a Welch's test?

b) Conduct a t-test (whichever one you decided was most appropriate) to determine whether the difference in physiological development between the infants in the circulatory arrest group and the low-flow bypass group is statistically significant.

c) Conduct a t-test (whichever one you decided was most appropriate) to determine whether the difference in mental development between the infants in the circulatory arrest group and the low-flow bypass group is statistically significant.

d) Calculate the 95% confidence intervals for these two tests. Interpret these in terms of the context of the study. What does the confidence interval mean? Which group did better?

e) If your child had to have open-heart surgery as an infant, which treatment option would you prefer? Why?

Answers for computing two sample t-test and confidence interval by hand

```
#hypothesis test

SDpooled= sqrt(((((84-1)*253.6135^2)+((85-1)*197.3636^2))/(84+85-2))
SDpooled
```

```
## [1] 227.0686
```

```
SE_d= SDpooled*sqrt((1/84)+(1/85))
SE_d
```

```
## [1] 34.93424
```

```
#test statistic
t= (181.8706-260.2976)/SE_d
t
```

```
## [1] -2.244989
```

```
df=84+85-2
df
```

```
## [1] 167
```

```
#p-value
2*pt(t, df=df)
```

```
## [1] 0.02608141
```

```
#Confidence interval

qt(c(0.025,0.975), df=df) #t for 95% CI with 167 df
```

```
## [1] -1.974271  1.974271
```

```
-78.427+ qt(c(0.025,0.975), df=df)*SE_d #formula for CI
```

```
## [1] -147.39666   -9.45734
```

Answers for heart study

```
#part A

by(heart$PDI, heart$Treatment, sd)
```

```
## heart$Treatment: Circulatory arrest
## [1] 16.488
## ------------------------------------------------------------
## heart$Treatment: Low-flow bypass
## [1] 14.68527
```

```
by(heart$MDI, heart$Treatment, sd)
```

```
## heart$Treatment: Circulatory arrest
## [1] 16.56448
## ------------------------------------------------------------
## heart$Treatment: Low-flow bypass
## [1] 14.57256
```

```
#part B

t.test(heart$PDI ~ heart$Treatment, var.equal = T)
```

```
##
##  Two Sample t-test
##
## data:  heart$PDI by heart$Treatment
## t = -2.2385, df = 141, p-value = 0.02676
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -11.0232390  -0.6840017
## sample estimates:
## mean in group Circulatory arrest    mean in group Low-flow bypass
##                         91.91781                         97.77143
```

```
#part C

t.test(heart$MDI ~ heart$Treatment, var.equal = T)
```

```
##
##  Two Sample t-test
##
## data:  heart$MDI by heart$Treatment
## t = -1.2696, df = 141, p-value = 0.2063
## alternative hypothesis: true difference in means is not equal to 0
## 95 percent confidence interval:
##  -8.484009  1.848393
## sample estimates:
## mean in group Circulatory arrest    mean in group Low-flow bypass
##                         103.0822                         106.4000
```

```
#part D

#found in the t.test output

#part E
```

Summary taken from the journal for comparison (some of their analyses were different, but our results should support the same conclusions):

Of the 171 patients enrolled in the study, 155 were evaluated. After adjustment for the presence or absence of a ventricular septal defect, the **infants assigned to circulatory arrest, as compared with those assigned to low-flow bypass, had a lower mean score on the Psychomotor Development Index. The method of support was not associated with the prevalence of abnormalities on MRI scans of the brain, scores on the Mental Development Index.** Heart surgery performed with circulatory arrest as the predominant support strategy is associated with a higher risk of delayed motor development and neurologic abnormalities at the age of one year than is surgery with low-flow bypass as the predominant support strategy.