Homework # 1

Biostatistics 210

DUE October 2, 2018 (by 10:30am) to the TA mailbox near photocopy room near conference room 2600, Mission Hall. Contact: zara.Izadi@ucsf.edu for questions or issues

0. BACKGROUND

This assignment will give you the opportunity to compare a series of analyses for a simple dataset. The purpose is to give you practice in contrasting analyses and considering their (1) validity (unbiasedness of estimates, size of tests, coverage of confidence intervals), (2) efficiency (standard error of point estimates, power of tests, and width of confidence intervals) and (3) robustness (how methods perform when their key assumptions are incorrect).

The data setting is based on a clinical trial of corneal ulcers. All 500 patients are given antibiotic therapy and half are randomized to placebo drops and half are randomized to steriod drops. The primary outcome is the log minimum angle of refraction (logMAR) which is a measure of visual acuity. Patients have their logMAR measure at enrollment and at week 12.

1. DOWNLOAD

• Download the fake dataset `scut.dta` from the course website.

2. THE MODEL

The data that has mean log MAR which follows

	Mean log MAR	
	Baseline	Week 12
Placebo Drops	α	$\alpha + \beta_0$
Steroid Drops	α	$\alpha + \beta_0 + \beta_1$

based on this. The mean log is equal in the two groups at baseline (as expected in a clinical trial) and value is set to be α. The mean logMAR is the placebo group at week 12 is $\alpha + \beta_0$ in the placebo group and is $\alpha + \beta_0 + \beta_1$ in the steroid group at week 12.

The change in logMAR in the placebo group from baseline to week 12 is then given by $(\alpha + \beta_0) = \beta_0$. The mean difference in logMAR at week 12 between steroid and placebo

is given by $(\alpha + \beta_0 + \beta_1)-(\alpha + \beta_0) = \beta_1$. This is the difference that the study is designed to detect. -- the difference in average logMAR scores between the two groups at week 12. One other aspect of this data which we need to consider is the correlation structure. We will see an important aspect of analyzing such data is the magnitude of the correlation, rho, in the data.

3. ANALYSIS

We will examine three different ways of estimating this difference

1. A simple t-test (compares mean logMAR at week 12 between the two groups)
2. A change score t-test (this analysis calculates the change score from baseline to week 12 and then compares those scores between the two groups)
3. A mixed model which treats logMAR values as repeated measures data and models how logMAR scores change with time, treatment and a time-by-treatment interaction.

The data was simulated in a way which ensures that all of these should all estimate the same quantity -- β_1.

Q1: Among the 3 analysis, which would seem to be the most different in spirit from the other 3? Which, for you, seems to be simplest one to explain?

Read in the data

```
use scut.dta
```

The dataset has variables

`id`: Participant ID #
`logmar1`: The Global Deficit Score at baseline
`logmar2`: The Global Deficit Score at week 12
`rx`: Study Treatment (0=Placebo, 1 = Steroid)

You can quickly get the means in the 2 groups at the two timepoints using the table command

```
table rx, c(mean logmar1 mean logmar2)
```

You can also get a sense of the data using boxplots

```
graph box logmar1 logmar2, over(rx) scheme(s1color)
```

Analysis 1: t-test

```
ttest logmar2, by(rx)
```

Q2: What is the mean difference given by the t-test, can you identify it as a difference between two cells in the table of means? What is the two-sided p-value for the t-test?

Analysis 2: t-test on change score

First, we create variable diff we create a variable

```
gen diff=logmar2-logmar1
```

Tabulate the mean change

```
table rx, c(mean diff)
```

Q3: What is the mean change in logMAR from baseline to week 12 in each group?

```
ttest diff, by(rx)
```

Q4: What is the mean difference given by the t-test on differences? How does it differ from the one you got from the t-test under analysis 1? Why do they differ? What is the two-sided p-value for the test?

Analysis 3: Mixed effects Model

A final approach is to use all the outcome data by creating a longitudinal model. In such a case, the desired treatment effect is a treatment by time interaction.

First switch the data from “wide” to “long”

```
reshape long logmar , i(id)
xtset id
gen timepoint=_j-1
```

timepoint will be coded to 0=baseline, 1=week 12. The interaction term is

```
gen inter = timepoint*rx
```

and the mixed effects command is

```
xtmixed logmar rx timepoint inter || id:,
```

Q5: How do you interpret the results? How do they compare with the other models?

4. SIMULATION

It will be helpful to examine how these 4 analyses compare over many similar datasets. This will give us a sense of the bias, efficiency and power of the techniques.

Download the file

hw1-sim.do

from the course website.

In Stata, go to Window, Do file editor, open new do file

Then Open the File in the do file editor

The simulation allows the following to vary

nsim	the number of simulations to be performed
nobs	the number of people in the trial (1/2 placebo, 1/2 steroid)
rho	the correlation between logmars at baseline and wk 12
mu1	the mean logmar at baseline
mu2	the mean logmar at week 12 (placebo group)
sigma1	the SD of logmars at baseline
sigma2	the SD of logmars at week 12
beta:	the effect of steroid at week 12 *(mean difference in logMAR betw' steroid and placebo)*

The default values create a dataset which will resemble the one you have analyzed.

Run the simulation using the default values.

The simulation return the following for each simulated dataset

ttest:	treatment effect (estimate of beta) given by t-test in analysis 1
ptest	two-sided p-value given by t-test in analysis 1
power-ttest:	1=if ptest < 0.05, 0 otherwise
paired	treatment effect given by t-test in change score given in analysis 2
ppaired	two-sided p-value given by t-test in analysis 2
power-paired	1=if ppaired < 0.05, 0 otherwise

mxt	treatment effect from mixed model in analysis 4
pmxt	two-sided p-value given by mixed model in analysis 4
power-mxt	1=if pmixed < 0.05, 0 otherwise

Q7: Are all the method unbiased for estimating the coefficient beta (=-0.15)? What are the relative efficiency compared with the mixed model? Do any of the methods appear to given an identical estimate of the treatment effect?

Q8: Which method is the most powerful? Which is the least?

Q9: Modify the simulations so rho=0.50. How do your answers in Q7 and Q8 change?

Q10: Modify the simulations so rho=0.0. How do your answers in Q7 and Q8 change?