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PhD Course in Basic Biostatistics
Fall 2014

One (potential) solution

1. *Based on the results from Study A, how many should be included in each group to find a clinical difference of 1mg/l with a statistical power of 80%?*

Based on a two-sample comparison of mean difference of 1mg/l, standard deviation of 2.1 mg/l, and a significance level of 5% we derive that 70 individual in each group is required to obtain a statistical power of 80%.

2. *Which of the two measures (after-before) and (after/before) seem the most appropriate measure describing the change in the concentration of Tatsoib?*

The clinically important increase of 1mg/l suggests that absolute difference is the appropriate change in concentration of Tatsoib. However, since the data set include both before and after measurement we can from Bland-Altman plot decide which of the two measure of the change that most appropriate measure. Judging from the Bland-Altman plot of the concentration of Tatsoib (Figure 1) and the log-concentration of Tatsoib (Figure 2) it seems that the mean level and variations of the absolute difference is approximately the same for all individuals, hence the (after-before) change is the most appropriate measure describing the change in the concentration of Tatsoib.

Figure 1 Bland-Altman plot for the after-before change.

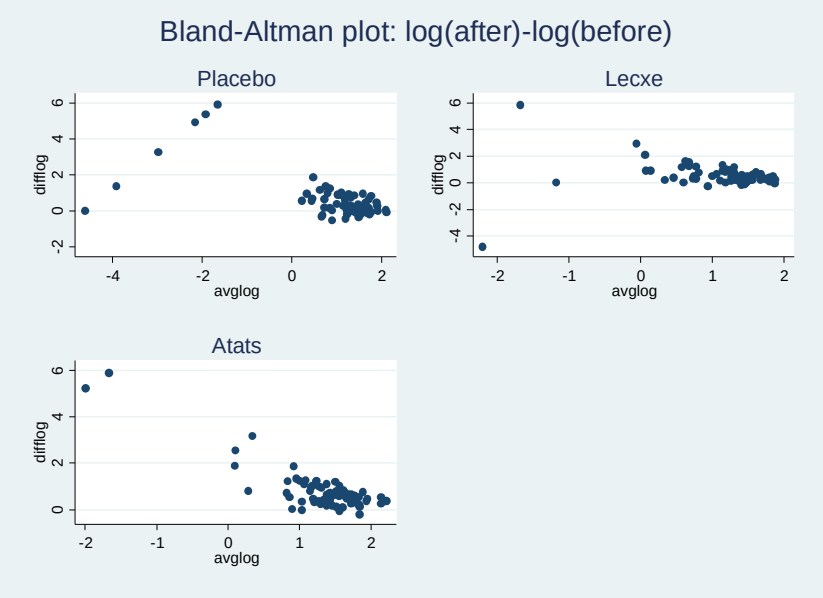

Figure 2 Bland-Altman plot for the after/before change based on the logarithm of both the before and after measurement.

3. *Compare the increase in Tatsoib of the Lecxe group to the placebo group. Similarly, compare the increase in Tatsoib of the Atats group to the placebo group. Create an overall test comparing the increase in Tatsoib in the three treatment group.*

QQ-plots confirm that the change in Tatsoib (after-before) follow approximately a normal distribution in all three treatment groups and the F-test accept the hypothesis of variance homogeneity.

The increase in Tatsoib is 0.63 (95% CI: 0.17; 1.08) mg/l higher in the Lecxe group compared to placebo, which is statistical significant (p=0.008). Similarly, the increase in Tatsoib is 1.64 (95% CI: 1.16;2.11) mg/l higher in the Atats group compared to placebo, which is however statistical significant (p<0.001).

An overall test comparing the increase in Tatsoib in the three treatment groups can be performed using a one-way anova or a linear regression model. In any case there is a highly significant difference in the mean increase in Tatsoib (p<0.001).

4. *Compare the increase in Tatsoib of the Lecxe group to the Atats group.*

The increase in Tatsoib is 1.01 (95% CI: 0.55;1.47) mg/l higher in the Atats group compared to Lecxe, which is statistical significant (p<0.001).

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5. *Is the increase in Tatsoib of the Lecxe group in the current study (Study B) compatible to the Tatsoib increase in the first study (Study A)?*

The increase in Tatsoib in study B is 1.64 (95% CI: 1.33;1.96) and in the first study (Study A) it was 1.13 (95%CI: 0.46-1.80). These are two independent samples; since one estimate is in the other confidence interval, there is no significant difference in the mean increase in *Tatsoib of Lecxe* in the two studies.

6. *Quantify the increase in Tatsoib of the Lecxe group compared to the placebo group for patients younger than 50 years.*
Quantify the increase in Tatsoib of the Lecxe group compared to the placebo group for patients aged 50 years and older.
Repeat this analysis for the Atats drug.

The increase in Tatsoib is 0.37 (95% CI: -0.16; 0.90) mg/l higher in the Lecxe group compared to placebo for patients younger than 50 years, which is however not statistical significant (p=0.17). Similarly, the increase in Tatsoib is 1.10 (95% CI: 0.22;1.97) mg/l higher in the Lecxe group compared to placebo for patients aged 50 years and older, which is statistical significant (p=0.02).

The increase in Tatsoib is 1.44 (95% CI: 0.87; 2.01) mg/l higher in the Atats group compared to placebo for patients younger than 50 years, which is statistical significant (p<0.001). Similarly, the increase in Tatsoib is 1.98 (95% CI: 1.11;2.86) mg/l higher in the Atats group compared to placebo for patients aged 50 years and older, which is statistical significant (p<0.001).

7. *Compare the difference between Lecxe and Atats for patients younger than 50 years to patients aged 50 years and older.*

The increase in Tatsoib between the Lecxe and the Atats group for patients younger than 50 years is 0.18 (95%CI: -0.77; 1.14) higher that for patients aged 50 years and older, which is not statistical significant (p=0.71).

8. *Estimate and compare the drop-out frequency between the three treatment groups.*

The frequency of dropout was in the placebo group 2.5% (95% CI: 0.3%-8.7%), in the Lecxe group 11.3% (95% CI: 5.3%-20.3%) and in the Atats group 3.8% (95% CI: 0.8%-

10.6%). There was no statistical significant different in the drop-out rates (p=0.07, Fishers exact test).

9. *Write a brief summary of your analyses and conclusions.*

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Do-file

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**********************************************
* Solution.
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cd "D:\Teaching\BasalBiostat\Exam"
capture log close
log using "Solution.txt", replace text

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* Question 1.
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sampsi  0 1 , sd1(2.1) power(0.80)


use tatsoib2, clear

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* Question 2.
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gen diff=after-before
gen avg=(after+before)/2
scatter after before if(group==0) , title("Placebo") name(graph1, replace)
scatter after before if(group==1) , title("Lecxe") name(graph2, replace)
scatter after before if(group==2) , title("Atats") name(graph3, replace)
graph combine graph1 graph2 graph3
graph drop graph1 graph2 graph3

* Bland-Altman: after-before.
scatter diff avg if(group==0) , title("Placebo") name(graph1, replace)
scatter diff avg if(group==1) , title("Lecxe") name(graph2, replace)
scatter diff avg if(group==2) , title("Atats") name(graph3, replace)
graph combine graph1 graph2 graph3 , title("Bland-Altman plot: after-before")
graph drop graph1 graph2 graph3

* Bland-Altman: after/before.
gen logbefore=log(before)
label variable logbefore "Log before Tatsoib in mg/l"
gen logafter=log(after)
label variable logafter "Log after Tatsoib in mg/l"
gen difflog=logafter-logbefore
gen avglog=(logafter+logbefore)/2
scatter difflog avglog if(group==0) , title("Placebo") name(graph1, replace)
scatter difflog avglog if(group==1) , title("Lecxe") name(graph2, replace)
scatter difflog avglog if(group==2) , title("Atats") name(graph3, replace)
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graph combine graph1 graph2 graph3 , title("Bland-Altman plot: log(after)-log(before)")
graph drop graph1 graph2 graph3


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* Question 3.
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qnorm diff if(group==0), title("Placebo") name(graph1, replace)
qnorm diff if(group==1), title("Lecxe") name(graph2, replace)
qnorm diff if(group==2), title("Atats") name(graph3, replace)
graph combine graph1 graph2 graph3
graph drop graph1 graph2 graph3
sdtest diff if(group==0|group==1), by(group)
ttest diff if(group==0|group==1), by(group)
sdtest diff if(group==0|group==2), by(group)
ttest diff if(group==0|group==2), by(group)
regress diff ib0.group
test 1.group 2.group


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* Question 4.
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sdtest diff if(group==1|group==2), by(group)
ttest diff if(group==1|group==2), by(group)


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* Question 5.
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ttest diff=0 if(group==1)


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* Question 6.
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sdtest diff if( (group==0|group==1) & (age<50)), by(group)
ttest diff if( (group==0|group==1) & (age<50)), by(group)
sdtest diff if( (group==0|group==1) & (age>=50)), by(group)
ttest diff if( (group==0|group==1) & (age>=50)), by(group)

sdtest diff if( (group==0|group==2) & (age<50)), by(group)
ttest diff if( (group==0|group==2) & (age<50)), by(group)
sdtest diff if( (group==0|group==2) & (age>=50)), by(group)
ttest diff if( (group==0|group==2) & (age>=50)), by(group)
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* Question 7.
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ttest diff if( (group==1|group==2) & (age<50)), by(group)
ttest diff if( (group==1|group==2) & (age>=50)), by(group)
gen age50=(age>=50)
regress diff i.group##i.age50 if(group==1 | group==2)


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* Question 8.
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gen missing=(after==.)
ci missing if(group==0), binomial
ci missing if(group==1), binomial
ci missing if(group==2), binomial
tabu missing group, exact expected chi2

log close
```