HW4 (Due: May 2)

1. Let us define the overall mean by:
2. What is the variance of ? Derive the formula.

[Hint: =

Or check the variance of a linear combination!]

1. Assume the constant variance (i.e., var(Yij)=σ2). Then the variance formula in a. is reduced to what?
2. Assume the same number of observations (i.e., ni=n) and correlation is exchangeable or equal (i.e., ρjk=ρ). Then the variance formula in b. is reduced to what?
3. What is the variance of , if N\*n observations are independent?
4. Compare the formula in c. and S220, and comment on implication of study design.

[Remark: There is a special name for the part of the formulae in c. vs. d. (or check S220) because this commonly plays a role in statistics, including here and multiple linear regression/multicollinearity. Think about the name!]

SEE ATTACHED RESPONSE AT THE END

1. Reproduce Tables 19, 20, 21 and 22 by computer and/or hand. What are differences and equivalences in these tables?

Table 19:

This is the response profile analysis from previous HW’s.

Coefficients:

Value Std.Error t-value p-value

(Intercept) 26.272 0.7102929 36.98756 0.0000

groupA 0.268 1.0045059 0.26680 0.7898

week1 -1.612 0.7919199 -2.03556 0.0425

week4 -2.202 0.8149021 -2.70217 0.0072

week6 -2.626 0.8885253 -2.95546 0.0033

groupA:week1 -11.406 1.1199438 -10.18444 0.0000

groupA:week4 -8.824 1.1524456 -7.65676 0.0000

groupA:week6 -3.152 1.2565645 -2.50843 0.0125

Table 20…this was hard, as the code on the website had a misleading line:

This is constraining group means to be equal at baseline (i.e. equal intercept)

Coefficients:

Value Std.Error t-value p-value

(Intercept) 26.406000 0.4998905 52.82357 0.0000

I(week == 1)TRUE -1.644501 0.7824043 -2.10186 0.0362

I(week == 4)TRUE -2.231356 0.8073816 -2.76369 0.0060

I(week == 6)TRUE -2.642065 0.8864610 -2.98046 0.0031

I(week == 1 & group == "A")TRUE -11.340999 1.0931205 -10.37488 0.0000

I(week == 4 & group == "A")TRUE -8.765289 1.1312579 -7.74827 0.0000

I(week == 6 & group == "A")TRUE -3.119870 1.2507769 -2.49435 0.0130

This is similar to response profile analysis, but equal means at baseline are assumed here. Only OK is randomized trial or the assumption of equal means at baseline is a valid one. Point estimates are very similar, but more precise, as there are less parameters to estimate.

Table 21:

This is an analysis of changes from baseline

Coefficients:

Value Std.Error t-value p-value

(Intercept) -1.612 0.7919227 -2.035552 0.0427

groupA -11.406 1.1199478 -10.184403 0.0000

week4 -0.590 0.6426966 -0.918007 0.3594

week6 -1.014 0.9343128 -1.085290 0.2787

groupA:week4 2.582 0.9089103 2.840764 0.0048

groupA:week6 8.254 1.3213178 6.246794 0.0000

This changes interpretation, as all coefficients refer to changes from baseline. As an example, the test of group X time interaction is now a test of parallel profiles for the changes from baseline. Also, the test of the group effect is now testing if changes from baseline differ between groups at occasion 2. Also, to test the main hypothesis of parallelism of profiles, we need to do a joint test of the main effects of group and group X time interaction. This is equivalent to the test of parallelism in regular response profile analysis. A final note, all subjects with missing values at baseline will not be included in the analysis, hence this approach could potentially reduce power (best case) or bias the estimates of effect if there are subjects with missing values at baseline

Table 22:

This table presents the results of an analysis of adjusted changes from baseline

Coefficients:

Value Std.Error t-value p-value

(Intercept) -1.638195 0.7766433 -2.109327 0.0358

cbaseline -0.195482 0.0938963 -2.081889 0.0382

groupA -11.353611 1.0984836 -10.335713 0.0000

week4 -0.590000 0.6427036 -0.917997 0.3594

week6 -1.014000 0.9343107 -1.085292 0.2787

groupA:week4 2.582000 0.9089202 2.840733 0.0048

groupA:week6 8.254000 1.3213149 6.246808 0.0000

As before, the test of parallelism of profiles is a joint test of group and group X time interaction. This analysis is more efficient than the one before, as by adjusting baseline it gains precision. By adjusting by baseline it also has the drawback that subjects with missing values at baseline will be excluded, with the same consequences as explained before.

1. In S230, a Wald test with df=3 is mentioned. Conduct this test (i.e., codes and output).

Code is in the R file and properly commented

Wald test

Model 1: D ~ cbaseline + group \* week

Model 2: D ~ cbaseline + week

Res.Df Df Chisq Pr(>Chisq)

1 287

2 290 -3 111.48 < 2.2e-16 \*\*\*

Result is virtually the same as the one in SAS (111.13)

1. Reproduce Tables 23, 24 and 25 and comment on models/results.

Table 23:

This is a linear trend model of FEV1

Coefficients:

Value Std.Error t-value p-value

(Intercept) 3.507313 0.10037773 34.94115 0.0000

smoker -0.261701 0.11509916 -2.27370 0.0233

time -0.033224 0.00306635 -10.83513 0.0000

smoker:time -0.004998 0.00352539 -1.41784 0.1566

There's a significant difference at baseline and a significant time effect. The main interest of the study, the interaction between smoking status and time was not significant, meaning that the profiles between groups are parallel (i.e. no significant effect of smoking status on FEV decay)

Table 24 (LRT):

Testing if the model with the linear trend has a significantly worse fit (lower likelihood) than the model with the quadratic trend

Model df AIC BIC logLik Test L.Ratio p-value

m7 1 34 305.1824 463.2038 -118.5912

m6 2 32 302.4609 451.1869 -119.2305 1 vs 2 1.278513 0.5277

Here the quadratic trend dos not significantly improve the fit of the model (i.e. increases the likelihood of the data)

Table 25:

These are the results of a piecewise linear model with knot at week 1

Coefficients:

Value Std.Error t-value p-value

(Intercept) 26.342207 0.4991198 52.77733 0.0000

week -1.629603 0.7817592 -2.08453 0.0378

week1 1.430494 0.8777585 1.62971 0.1040

trt.week -11.249985 1.0924522 -10.29792 0.0000

trt.week1 12.582249 1.2278544 10.24735 0.0000

The results show that the profiles are significantly not parallel between the groups, both before and after week 1.

1. Conduct the model comparison (i.e., piecewise linear vs. quadratic trend) described in S266.

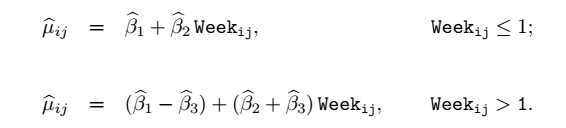
Here’s the piecewise linear model deviance: 2436.226 (df=15)

Here’s the quadratic trend model deviande: 2511.683 (df=15). This is slightly smaller than in the slide (2551.7)

1. Show how to compute estimated vs. observed means in Table 26. [You don’t need to verify all numbers. Show 2-3 entries and/or explain how to derive them.]

To compute the estimated means (the observed is just the mean of each stratum, so I won’t give an example of that) we must use the regression coefficients from the model.

For the placebo group this is:



Hence:

Placebo @ week 0 = 26.342207 - 1.629603 X 0 = 26.342207 ~ 26.3

Placebo @ week 1 = 26.342207 – 1.629603 X 1 = 24.7126 ~ 24.7

Placebo @ week 3 = 26.342207 - 1.430494 + (-1.629603 + 1.430494) X 4 = 24.11528 ~ 24.1

