

## EXAM – SOLUTIONS

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For some questions, the solutions below give MORE details than were required to get full credit (all points). Questions are worth 10 points each; only 10 of the 12 questions were to be answered.

### APPLICATION

- Summary statistics on page 9 indicate that the mean serum ferritin is higher in the high dose group compared to the low dose group.
  - The plot on page 10 indicates that serum ferritin decreased across the study months in the low dose group, but increased across the study months in the high dose group.
- Several answers were possible, including those shown below.

(a) Toeplitz does seem reasonable

- time points are equally spaced
- for both groups because the correlations appear to decrease across lags.

However, Toeplitz does not seem reasonable

- for either group because the correlations do not appear very stable within lag
- for either group because the variance appears to be increasing across months.

Toeplitz seems more appropriate for the high dose group, because the within-lag correlations seem more stable for this group.

(b) AR(1) does seem reasonable

- time points are equally spaced
- for both groups because the correlations decay across increasing lag about as fast as AR(1) requires. (Example: if the lag 1 correlation is about 0.78, then the lag 2 correlation is forced to be  $(0.78)^2 = 0.61$ , the lag 3 correlation is forced to be  $(0.78)^3 = 0.47$ , and the lag 4 correlation is forced to be  $(0.78)^4 = 0.37$ .)

However, AR(1) does not seem reasonable

- for either group because the variance appears to be increasing across the months.

AR(1) seems a bit more appropriate for the high dose group, because the correlations decay closer to what AR(1) requires.

- In order to test for the GROUP effect, we need to compare model # 1 to model # 3, and model # 2 to model # 4.

- (a) # 1 vs. # 3:  $T^* = 2140.0 - 2133.4 = 6.6$  with degrees of freedom  $r = 12 - 6 = 6$ . Since  $T^* < \chi_{6,0.95}^2 = 12.59$  we fail to reject and conclude that model # 1 is sufficient.
- (b) # 2 vs. # 4:  $T^* = 2089.2 - 2066.3 = 22.9$  with degrees of freedom  $r = 42 - 21 = 21$ . Since  $T^* < \chi_{21,0.95}^2 = 32.67$  we fail to reject and conclude that model # 2 is sufficient.

Thus, a **GROUP** effect for treatment is not needed.

- 4. A. Women in the high dose iron supplement group had significantly higher average serum ferritin levels than women in the low dose group (LS means 46.77, st.dev. 1.54, vs. 38.70, st.dev. 1.54, respectively,  $t^*=3.67$ ,  $p=0.0006$ ).
- B. Women in the high dose iron supplement group had an increasing trend in serum ferritin across the study (slope est. 2.37) while women in the low dose group had a decreasing trend (slope est. -1.80,  $t^*=5.62$ ,  $p<0.0001$ ).
- 5. Several answers were possible, including those shown below.
  - (a) The plot on page 7 shows one woman in the high dose group whose trend across time is strongly decreasing, in contrast to the other women in that group; her last two observations in particular seem to be outlying. These two observations can also be seen in the cluster of points that fall far below the diagonal in the plot on page 21, and in the points with large negative residual values in both plots on page 23.
  - (b) The average trends across time are approximately linear for both groups, as shown in the plot on page 7. (Note: a GLM does NOT require that the women's individual trends also be linear.)
  - (c) The plot on page 22 indicates that the model fitted variances ("fitted Sigma") follow the estimated OLS variances quite closely. The model fitted correlation matrix shown on page 13 seems like a good approximation to the two OLS correlation matrices shown on page 9.

## CONCEPTS

- 6. AIC and BIC can both be used to compare non-nested covariance structures. The model with the smaller AIC (or smaller BIC or both) would be the preferable model.
- 7. We need a test of the treatment effect on the outcome at baseline. Because our time variable is coded as 0,1,2,3,4,5 (rather than 1,2,3,4,5,6), the test of the main effect `trt` is equivalent to this test. Alternatively, we could ask for the LS means for the treatment groups at time 0 (the `AT visit=0` and `DIFF` options in the `LSMEANS` statement) and just pull out the test of this difference. Alternatively, we could pull out the observations corresponding to the outcome data at time 0 and do a 2-sample t-test.

8. (a) Toeplitz is no longer a reasonable structure to consider, because Toeplitz requires that correlations be constant within each diagonal of the covariance matrix. With equally spaced time points, each diagonal corresponds to one lag, so any observations that are the same lag apart have the same correlation. With unequally spaced time points, each diagonal contains correlations from multiple lags, so forcing those correlations to be equal does not make sense.
  - (b) Unstructured is still a reasonable structure to consider, since all correlations (no matter what lag) are allowed to take whatever magnitude the data indicate.
9. There are several possible answers, including those shown here. We could exclude all of her observations from the data, re-run the model, and see if we reach a different conclusion for either of the research questions. We could exclude only her two outlying observations, re-run the model, and see if we reach a different conclusion for either of the research questions. We could examine the influence diagnostic statistics available in PROC MIXED and use those to decide whether or not any of her observations should be excluded. We could investigate whether there was a data entry error. We could investigate whether she should have been excluded from the trial based on the study's inclusion/exclusion criteria. We could investigate whether she complied with the protocol (perhaps she stopped taking her supplement). We could investigate whether she experienced a health outcome that could have impacted her serum ferritin levels. We could investigate whether there was some other important covariate that might explain her unusual trajectory.
10. There are several possible answers, including those shown here. A repeated measures ANOVA assumes a compound symmetry covariance structure; that does not seem appropriate based on the OLS correlation matrices shown on page 9. A repeated measures ANOVA does not directly produce slope estimates, because it fits a separate mean at each time point for each group, rather than a slope across time for each group; a linear contrast across the time points would have to be estimated to get at a slope.
11. Only one of the following answers was needed to get full credit: This makes sense because  $\hat{\alpha}$  is a complicated linear combination of the outcome values  $Y$  which are assumed normally distributed; linear combinations of normally distributed things are also normally distributed. This makes sense also because statistical theory says that maximum likelihood estimates (which  $\hat{\alpha}$  is) are asymptotically normally distributed.
12. (a) Compound symmetry seems reasonable since it allows for estimation of a common correlation among all women within each center. Independence (variance components) will be reasonable if any within-center correlation is negligible. No other structures are reasonable because there is no inherent ordering of the women within clinics.
  - (b) Note that the `visit` main effect and interaction are no longer needed.

```
proc mixed;
  class center trt;
  model ironchange = pregnancy anemia trt;
```

```
repeated id / sub=center type=cs;
```

## EXTRA CREDIT

1. The options `s`, `r`, and `rcorr`, and the `class` and `lsmeans` statements, did not need to be shown to get full credit.

```
proc mixed data=dat;  
  class cvisit id trt;  
  model iron = anemia pregnancy trt visit trt*visit / s;  
  repeated cvisit / sub=id type=un group=trt r=1,4 rcorr=1,4;  
  lsmeans trt / pdiff tdiff;  
run;
```