**BIOS6643 HW3 Trent Hawkins**

**NOTE:** All the models presented in this analysis used the REML method of estimation. It was later discovered that model AIC can only be compared across all these models using the ML method. Please note that all decisions and interpretations were made in the context of the former method, and therefore cannot be considered meaningful.

Consider the Fitness data that includes 3 groups (low intensity=a, high intensity=b, control=c). Group and time will be modeled as class variables, a group\*time interaction will be included, and the error covariance matrix will be fit using a first-order autoregressive [AR(1)] structure. There are no random effects in this model. Note that you can either use PROC MIXED in SAS or the gls function in R (nlme package) to fit the model. NOTE: use Satterthwaite DDF, mainly so we’re all on the same page. To do this in SAS, use ddfm=satterth as an option in the MODEL statement. Please include your SAS and/or R code in an Appendix.

* 1. Write the less-than-full-rank (LTFR) statistical model, i.e., include all levels of class variables, letting α denote group, τ denote time and γ denote interaction; let *h* indicate group, *i* indicate subject and *j* indicate time. Include distributions, assumptions, etc. for the model.

Where:

This model assumes where is some covariance matrix that is imposed (in this case an AR(1) structure).

Since the model is less than full rank, there will be linear dependencies in the design Matrix (X), making it non-estimable. To deal with these linear dependencies, SAS will use a generalized inverse to make the calculation of possible.

* 1. How many (a) fixed-effect parameters and (b) covariance parameters are in the LTRF model?

There are a) 24 fixed-effect parameters and b) 2 covariance parameters,

* 1. Fit the model using SAS or R. How does this model that uses an AR(1) structure compare to the random intercept model (with the same fixed effects), based on AIC goodness of fit? (What I call the ‘random intercept model’ has a random intercept but simple error covariance structure – i.e., you do not need to specify the latter.)

|  | **AR(1) Structure** | **Random Intercept (Simple Structure)** |
| --- | --- | --- |
| **-2 Res Log Likelihood** | 377.8 | 396.6 |
| **AIC (Smaller is Better)** | 381.8 | 400.6 |
| **AICC (Smaller is Better)** | 382.0 | 400.8 |
| **BIC (Smaller is Better)** | 383.2 | 402.0 |

The model using the AR(1) structure has a smaller AIC at 381.8, indicating that it fits the data better than the random intercept model. It should be noted that these models were fit using ***REML*** method of estimation.

* 1. Write out the form of **V***i*=*Var*(**Y***i*) for the 2 models in Q3 (should be 5×5 matrices). [Note for SAS: you can also determine what these matrices look like numerically in SAS by including the *v* option (after the slash) if there is a RANDOM statement, and an *r* option in the REPEATED statement if there is no random statement. Similarly, the *vcorr* and *rcorr* options put these in terms of correlation matrices.]

AR(1) Structure:

Where and The correlation between two evenly spaced time points

Random Intercept (Simple) Structure:

* 1. Based on the model in #1-3 (using AR(1) structure on errors), determine coefficients for the following customized tests/estimates, and run then with SAS or R to obtain results.
     + 1. Write an estimate (or contrast) to determine the change from baseline to 4 weeks (4-0wk) for group a.
       2. Write an estimate (or contrast) to determine the change from baseline to 4 weeks (4-0wk) for group b.
       3. Write an estimate (or contrast) to compare change over time (4-0wk) for group a versus b.
       4. Write an estimate (or contrast) to compare the average of programs b vs. c, but only for the last 2 weeks.
       5. Write a contrast for the group\*time interaction for group b (high intensity) versus c (control).

| **Estimates** | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Label** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** | **Alpha** | **Lower** | **Upper** |
| **group a (4-0 wk)** | 16.2000 | 3.3274 | 58.2 | 4.87 | <.0001 | 0.05 | 9.5401 | 22.8599 |
| **group b (4-0 wk)** | 24.4000 | 3.3274 | 58.2 | 7.33 | <.0001 | 0.05 | 17.7401 | 31.0599 |
| **group a vs b (4-0 wk)** | -8.2000 | 4.7057 | 58.2 | -1.74 | 0.0867 | 0.05 | -17.6186 | 1.2186 |
| **group b vs c (avg last 2 wk)** | 25.7000 | 5.4377 | 16.2 | 4.73 | 0.0002 | 0.05 | 14.1824 | 37.2176 |

| **Contrasts** | | | | |
| --- | --- | --- | --- | --- |
| **Label** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| b and c interaction | 4 | 47.8 | 8.55 | <.0001 |

These estimate and contrast statements test the following null hypotheses:

Group a (4-0 wk):

Group b (4-0 wk):

Group a vs b (4-0 wk):

Group b vs c (avg last 2 wk):

Group B and C interaction: for all values of j

Interpretation:

Group a (4-0 wk): From baseline to 4 weeks, the low intensity treatment group sees a 16.2 (95% CI: 9.54, 22. 86) unit increase in fitness. At p < 0.0001, we may reject H­0.

Group b (4-0 wk): From baseline to 4 weeks, the high intensity treatment group sees a 24.4 (95% CI: 17.74, 31.06) unit increase in fitness. At p < 0.0001, we may reject H­0.

Group a vs b (4-0 wk): The confidence interval for this estimate overlaps 0 (p = 0.087), so we fail to reject the null hypothesis that the change from baseline to 4 weeks for the low to high-treatment groups is significantly different from 0.

Group b vs c (avg last 2 wk): The average for the high-treatment group is 25.7 (95% CI: 14.18, 37.22) units higher than that of the control group. At p = 0.0002 we reject the null hypothesis that the average is the same between the two groups.

Group B and C interaction: At p < 0.0001, we can conclude that the interaction with time is different for the high intensity and control groups.

* 1. Using the model determined from Q3 to be the best in terms of AIC, refit a model considering time as a continuous variable. What order of polynomial is sufficient? How do you decide? Include group\*time interactions, up to the specified order. E.g., if quadratic is sufficient, include group\*time and group\*time2 as predictors in addition to group and time. Based on all the models you have fit so far, which one would be your ‘final’ model, e.g., if you were to submit a paper on it?

|  | **AR(1) Structure (Time as Class)** | **Random Intercept (Simple Structure)** | **AR(1) Structure (Cont. Linear)** | **AR(1) Structure (Cont. Quadratic)** | **AR(1) Structure (Cont. Cubic)** |
| --- | --- | --- | --- | --- | --- |
| **-2 Res Log Likelihood** | 377.8 | 396.6 | 425.4 | 411.1 | 411.3 |
| **AIC (Smaller is Better)** | 381.8 | 400.6 | 429.4 | 415.1 | 415.3 |
| **AICC (Smaller is Better)** | 382.0 | 400.8 | 429.6 | 415.3 | 415.5 |
| **BIC (Smaller is Better)** | 383.2 | 402.0 | 430.8 | 416.5 | 416.7 |

Based the AIC for each of the models fit in this exercise (up to cubic for continuous), it appears that the AR(1) structure with time as a class variable has the best fit to the data (AIC = 381.8). The ‘final’ model comes down to the question of interest. If the investigator is specifically interested in a non-linear trend in the data, than the AR(1) Structure with a quadratic term for time (AIC = 415.1) will be the best fit for the data. The same model with a cubic term for time has similar AIC, but I would caution against estimating extra parameters if the model fit does not benefit greatly. It should be noted that these models were all fit using the ***REML*** method of estimation.

| **Contrasts** | | | | |
| --- | --- | --- | --- | --- |
| **Label** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| linear | 1 | 58 | 51.90 | <.0001 |
| quadratic | 1 | 46.1 | 4.88 | 0.0322 |
| cubic | 1 | 44.4 | 0.28 | 0.5975 |
| quartic | 1 | 44 | 0.02 | 0.8785 |
| lxl | 2 | 58 | 12.83 | <.0001 |
| qxq | 2 | 46.1 | 4.78 | 0.0130 |
| cxc | 2 | 44.4 | 0.59 | 0.5596 |
| 4x4 | 2 | 44 | 0.23 | 0.7984 |

The table above tests for non-linear effects of time on the outcome and the interactions between time and program up to quartic effects. The table shows that time and the program-by-time fixed effects have a statistically significant quadratic relationship with the outcome (p = 0.032 & p = 0.013). Models that treat time as a continuous variable should add up-to a quadratic effect.

* 1. Write a brief (half page) summary of your findings overall, including the statistical lingo that you would ordinarily include in a research article. (Talk to me if you have questions about this.) In your write up, feel free to include other tests if you’d like. For example, in 6e you did an interaction test for program b versus c; you could compare a and c or a and b. This is not necessary for full credit, but might help in your learning and to make a more complete write up..

**Full Results:**

| **Estimates** | | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Label** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** | **Alpha** | **Lower** | **Upper** |
| **group a (4-0 wk)** | 16.2000 | 3.3274 | 58.2 | 4.87 | <.0001 | 0.05 | 9.5401 | 22.8599 |
| **group b (4-0 wk)** | 24.4000 | 3.3274 | 58.2 | 7.33 | <.0001 | 0.05 | 17.7401 | 31.0599 |
| **group c (4-0 wk)** | 1.2000 | 3.3274 | 58.2 | 0.36 | 0.7197 | 0.05 | -5.4599 | 7.8599 |
| **group a vs b (4-0 wk)** | -8.2000 | 4.7057 | 58.2 | -1.74 | 0.0867 | 0.05 | -17.6186 | 1.2186 |
| **group b vs c (avg last 2 wk)** | 25.7000 | 5.4377 | 16.2 | 4.73 | 0.0002 | 0.05 | 14.1824 | 37.2176 |

| **Contrasts** | | | | |
| --- | --- | --- | --- | --- |
| **Label** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| b and c interaction | 4 | 47.8 | 8.55 | <.0001 |
| a and b interaction | 4 | 47.8 | 2.24 | 0.0782 |
| a and c interaction | 4 | 47.8 | 2.80 | 0.0362 |

Overall, the treatments compared in this experiment have a positive impact on fitness, but the relationship is made more complex by the different levels of the treatment and the interaction between time and treatment group. The low-intensity treatment group saw a 16.2 (95% CI: 9.54, 22. 86) unit increase in fitness from baseline to 4 weeks (p < 0.0001) and the high-intensity treatment group saw a 24.4 (95% CI: 17.74, 31.06) unit increase (p < 0.0001). The confidence interval for the control group overlapped 0 (p = 0.72). On average, however, there was not sufficient evidence to conclude that the high-intensity group saw added benefit over the low-intensity treatment group (p = 0. 087).

Regarding the program-by-time interaction effects, both the low and high-treatment groups had interactions with time that differed from the interaction effect of the control group. Again, however, the interactions with time comparing the low and high-treatment groups did not show evidence of being significantly different from one another (p = 0.08).

In model selection, we see that time and the program\*time interaction have quadratic relationships with the outcome (p = 0.032 and p = 0.013, respectively). In comparison with the model that treats time as a factor, however, the later has a better fit for the data in this experiment (AIC = 381.8).

In summary, the results of this experiment show that at least some exercise is more beneficial for fitness than some. There is not sufficient evidence to conclude that ramping up to high-intensity routines has a greater effect on fitness.