BIOSTATISTICS 667 (Fall 2019)
Homework 6

1. Read the study and data description in problem 5.1. The two groups will be identifed by $i = 1$ for placebo and $i = 2$ for high dose. The repeated measures will be identifed by $j = 1, \cdots, 5$. The obsevation times (0, 6, 12, 20, 24 months) will be denoted t_{ij}. The cell means in the 2×5 layout will be denoted η_{ij}.

   Use REML and Wald tests whenever possible and valid. Assume an unstructured matrix for the covariance of the response vector. For hypothesis testing describe your method, give the value of the test statistic, the degrees of freedom (if applicable) and the p-value.

   There are some missing outcomes in this problem which, depending on the reason for missingness, may lead to biased estimation. Ignore that aspect; missing data will be discussed later in this class.

   Do not present any computer code or output, not even in an appendix. Present only the relevant quantities.

   (a) Present simple descriptive statistics, tabular and/or graphical. Comment.

   (b) Fit the general two-way ANOVA model

   $$\eta_{ij} = \mu + \alpha_i + \beta_j + \gamma_{ij}.$$

   Apply the estimability restrictions $\alpha_1 = \beta_1 = \gamma_{1j} = \gamma_{i1} = 0$. [Note: If your software imposes other estimability restrictions, either reorder the rows and/or columns as necessary, or create your own dummy variables.] In this model, what are the parameters that represent the *treatment effect on the changes in mean cholesterol level over time*? Let δ be a vector that contains those parameters. Present parameter and standard error estimats of δ.

   (c) Within the model stated above, test the null hypothesis $\delta = 0$ against the alternative $\delta \neq 0$.

   (d) Fit a model similar to the general two-way ANOVA model but with the assumption that the two groups have the same mean at baseline. Present parameter and standard error estimats of δ. Within this model, test the null hypothesis $\delta = 0$ against the alternative $\delta \neq 0$.

   (e) Fit a model in which the mean is a quadratic function of time t_{ij} within each group, and the two groups have the same mean at baseline. Write the mean model and identify what represent the *treatment effect on the changes in mean cholesterol level over time*. Present parameter and standard error estimats of those effects. Test the hypothesis that those parameters are 0.

   (f) Let D_k, a 4×1 vector, denote the changes from baseline in subject k. The cell means (of D_k) in the 2×4 layout will be denoted ψ_{ij} Fit the general two-way ANOVA model

   $$\psi_{ij} = \mu + \alpha_i + \beta_j + \gamma_{ij}.$$

   Note that μ, α_i, β_j and γ_{ij} have a different meaning here compared to (b). Apply the estimability restrictions $\alpha_1 = \beta_1 = \gamma_{1j} = \gamma_{i1} = 0$. What are the parameters that represent the *treatment effect on the changes in mean cholesterol level over time*? Let λ be a vector that contains those parameters. Present parameter and standard error estimats of λ.

(g) Within the model stated above, test the null hypothesis $\lambda = 0$ against the alternative $\lambda \neq 0$.

(h) Add the baseline response as another column in the design matrix in the last model. Since this is a different model, the notation λ^* will be used instead of λ. Present parameter and standard error estimats of λ^*.

(i) Within the model stated above, test the null hypothesis $\lambda^* = 0$ against the alternative $\lambda^* \neq 0$ using a Wald test.

(j) Test the same hypothesis, $\lambda^* = 0$ against the alternative $\lambda^* \neq 0$, using a likelihood ratio test.

(k) What assumption(s) can guarantee that $\lambda = \lambda^*$, and hence guarantee that adjusting for baseline still provides a valid estimate of the target parameter λ?