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# ST 732, TEST 2 SOLUTIONS, SPRING 2007

**Please sign the following pledge certifying that the work on this test is your own:**

"I have neither given nor received unauthorized aid on this test."

Signature: ______________________________

Printed Name: ______________________________

*There are FIVE questions, all with multiple parts. For each part of each question, please write your answers in the space provided. If you need more space, continue on the back of the page and indicate clearly where on the back you have continued your answer. Scratch paper will be provided.*

*You are allowed ONE (1) SHEET of HANDWRITTEN NOTES (FRONT ONLY). Calculators are NOT allowed (you will not need one). NOTHING should be on your desk but this test paper, your one page of notes, and scratch paper given to you.*

*Points for each part of each problem are given in the left margin. TOTAL POINTS = 100.*

*In all problems, all symbols and notation are defined exactly as they are in the class notes.*

*If you are asked to provide a NUMERICAL ESTIMATE or EXPRESSION, and the ONLY WAY you can see to do this involves some arithmetic (e.g., adding or multiplying several numbers), YOU DO NOT HAVE TO DO THE ARITHMETIC. JUST GIVE THE EXPRESSION.*
*HOWEVER, if a numerical estimate IS AVAILABLE DIRECTLY from the output WITHOUT having to do arithmetic, I will only give partial credit if you do not recognize this.*

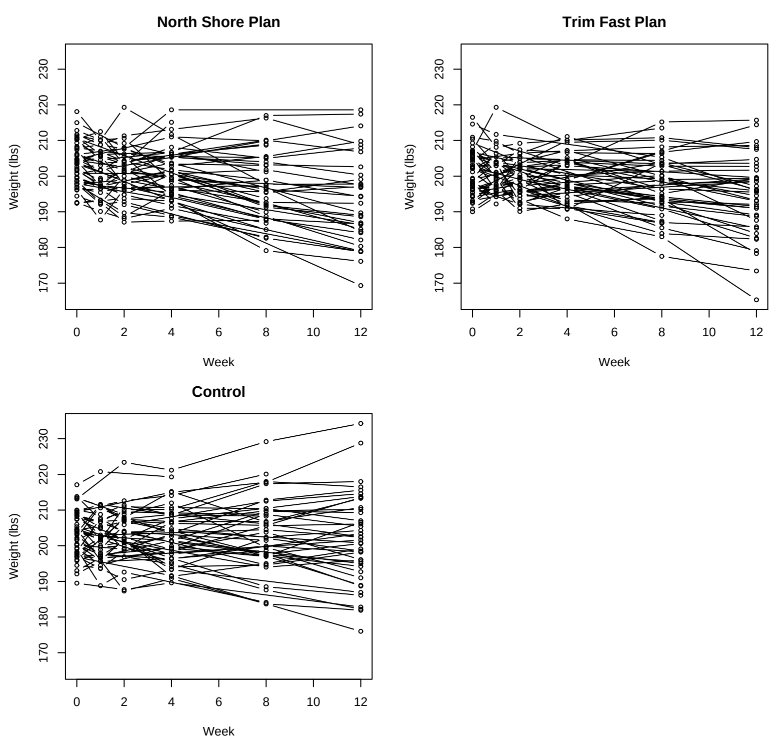
*If you believe it is IMPOSSIBLE to provide a numerical estimate or expression from what is provided, STATE THIS AND EXPLAIN.*

1. A study was conducted to compare the effectiveness of some popular weight loss programs when followed by overweight women between the ages of 20 and 40 years old, where "overweight" was defined as having a body mass index of 25 to 29.9. (Body mass index, or BMI, is a measure of body fat based on height and weight that is widely used to classify subjects into categories that may be associated with risk factors for cardiovascular and other diseases.) In the study, $m = 150$ women who were currently not following any diet plan were randomized as follows to three program groups:

   - Program 1: Subjects were instructed to follow the popular "North Shore" diet plan (50 subjects)
   - Program 2: Subjects were instructed to follow the popular "Trim-Quick" diet plan (50 subjects)
   - Program 3: Control group – subjects were instructed to continue with their usual eating habits (50 subjects).

   At baseline (week 0), the weights of the subjects were recorded immediately before they starting their assigned programs. Subjects then began following their assigned programs and were asked to return to the clinic at 1, 2, 4, 8, and 12 weeks thereafter to be weighed. A challenge with weight loss studies is that subjects may fail to show up for these visits or, worse, drop out of the study if they feel they have not lost sufficient weight. Thus, the investigators paid all subjects \$20.00 at each clinic visit to encourage them to continue to appear at the scheduled times. This tactic helped to keep the percentage of missed visits relatively low, although some women did miss some visits after the initial baseline one.

   The data set contains 742 weight measurements across the 150 subjects. The raw data are plotted below.




   Also recorded for each subject was an indicator of the subject's age (0 = 25 years old or less, 1 = older than 25).

The primary objective was to determine whether there is a difference in the pattern of weight change depending on which program women follow. A secondary objective was to conduct exploratory analyses to investigate a recent claim that age is associated with weight and with how well women will do in losing weight.

To address the primary objective, the investigators adopted the following statistical model. Let $Y_{ij}$ be the weight recorded for subject $i$, $i = 1, \ldots, m$, at time $t_{ij}$, where $j = 1, \ldots, n_i$ and $n_i \leq 6$ (recall that the planned visit times are 0, 1, 2, 4, 8, 12 weeks). Let

$$\begin{aligned}
\delta_{1i} &= 1 \text{ if subject } i \text{ was assigned to "North Shore" (program 1),} &&= 0 \text{ otherwise} \\
\delta_{2i} &= 1 \text{ if subject } i \text{ was assigned to "Trim-Quick" (program 2),} &&= 0 \text{ otherwise} \\
\delta_{3i} &= 1 \text{ if subject } i \text{ was assigned to "Control" (program 3),} &&= 0 \text{ otherwise}
\end{aligned}$$

The model is

$$Y_{ij} = \beta_{0i} + \beta_{1i} t_{ij} + e_{ij} \qquad (1)$$

$$\beta_{0i} = \beta_{00} + b_{0i}, \qquad \beta_{1i} = \beta_{11}\delta_{1i} + \beta_{12}\delta_{2i} + \beta_{13}\delta_{3i} + b_{1i}. \qquad (2)$$

*On page 6, you will find some SAS code and selected portions of its output. Use this to answer the remaining parts of this problem.*

[5 points] (a) The investigators fit (1), (2) under two different sets of assumptions on sources of variation. In the SAS program, the models resulting from each set of assumptions are called "Model I" and "Model II" (output for Model II is not given).

Explain in plain English (using no symbols) what is being assumed about variation and correlation under each model.

Both models are linear mixed effects models, and hence assumptions are made separately on the nature of variation and correlation due to among- and within-woman sources. Both models assume that each subject has her own "inherent" straight-line trajectory of weight over the course of the study. In Model I, the woman-specific intercepts and slopes are assumed to vary and covary in the same way in all three program populations. In contrast, in Model II, this variation and covariation is assumed to be possibly different across groups. Both models also assume that correlation due to within-woman sources is negligible. However, Model I assumes that the total variance due to the combined effects of all within-woman sources of variation ("fluctuations" in weight about the "inherent" trajectory and possible error in measuring weight) are the same in all three groups, while Model II assumes this variance is possibly different across groups.

*In the rest of the problem, assume Model I.*

[5 points] (b) Write down a numerical estimate of the variance of the "typical" or mean "inherent" weight at the start of the study for the population of women who went on to follow the "North Shore" diet (program 1).

There were two ways to interpret this question, and credit was given for either one. Some of you interpreted this as asking about $\beta_{0i}$, and thus reported $\text{var}(\beta_{0i}) = \text{var}(b_{0i})$. Under Model I, this quantity is the same in all three groups, so the estimate of this common quantity applies to women who went on to the "North Shore" diet. From the output, the estimate of this quantity is given in the `Covariance Parameter Estimates` table as UN(1,1) and is equal to 27.3760.

Others of you interpreted this as asking about the sampling variance of the estimator for $\beta_{00}$. From the `Solution for Fixed Effects` table, this is $0.4644^2$.

*Here is the model again for convenience:*

$$\begin{array}{lcll} \delta_{1i} & = & 1 \text{ if subject } i \text{ was assigned to "North Shore" (program 1),} & = \; 0 \text{ otherwise} \\ \delta_{2i} & = & 1 \text{ if subject } i \text{ was assigned to "Trim-Quick" (program 2),} & = \; 0 \text{ otherwise} \\ \delta_{3i} & = & 1 \text{ if subject } i \text{ was assigned to "Control" (program 3),} & = \; 0 \text{ otherwise} \end{array}$$

$$Y_{ij} = \beta_{0i} + \beta_{1i} t_{ij} + e_{ij} \tag{1}$$

$$\beta_{0i} = \beta_{00} + b_{0i}, \qquad \beta_{1i} = \beta_{11}\delta_{1i} + \beta_{12}\delta_{2i} + \beta_{13}\delta_{3i} + b_{1i}. \tag{2}$$

[5 points] (c) The primary study hypothesis was that the "typical" (mean) rate of weight change possibly differs in the population of overweight women depending on which program they follow.

In terms of symbols in model (1), (2), give a set of null and alternative hypotheses $H_0$ and $H_1$ that address this issue. Give numerical values of a test statistic and associated p-value appropriate for testing $H_0$ vs. $H_1$ and, based on them, state your conclusion regarding the strength of the evidence against $H_0$.

The question is whether or not $\beta_{11} = \beta_{12} = \beta_{13}$. This is addressed by `Contrast 'B'`. The test statistic is 13.06 or 6.53 – both have associated p-values $< 0.002$, which is very small. At any reasonable level of significance we would conclude that there is sufficient evidence to suggest that the rate of change of weight is different in at least one of the groups from the others.

[5 points] (d) Give a numerical estimate of the difference of population mean weight at the end of the study (12 weeks) between the "North Shore" (program 1) and control (program 3) programs. (You needn't provide a standard error.)

The population mean at 12 weeks for program 1 is $\beta_{00} + \beta_{11}(12)$, and that for program 3 is $\beta_{00} + \beta_{13}(12)$. Thus, the difference is $(\beta_{11} - \beta_{13})(12)$. There does not appear to be an estimate statement directly giving this value, but we can get a numerical expression from the `Solution for Fixed Effects` as

$$(-0.7384 + 0.09361)(12).$$

*Here is the model again for convenience:*

$$\begin{array}{lcllcl}
\delta_{1i} & = & 1 \text{ if subject } i \text{ was assigned to ``North Shore'' (program 1),} & = & 0 \text{ otherwise} \\
\delta_{2i} & = & 1 \text{ if subject } i \text{ was assigned to ``Trim-Quick'' (program 2),} & = & 0 \text{ otherwise} \\
\delta_{3i} & = & 1 \text{ if subject } i \text{ was assigned to ``Control'' (program 3),} & = & 0 \text{ otherwise}
\end{array}$$

$$Y_{ij} = \beta_{0i} + \beta_{1i} t_{ij} + e_{ij} \tag{1}$$

$$\beta_{0i} = \beta_{00} + b_{0i}, \qquad \beta_{1i} = \beta_{11}\delta_{1i} + \beta_{12}\delta_{2i} + \beta_{13}\delta_{3i} + b_{1i}. \tag{2}$$

[5 points] (e) An additional question that the investigators wanted to address was the long-standing issue of whether or not there is a difference in the rate at which women lose weight on average between the "North Shore" (program 1) and "Trim-Quick" (program 2) diet plans.

Is there evidence to suggest such a difference? (You need not state formal hypotheses.) From the output, provide numerical evidence (values of a test statistic and p-value) justifying your answer.

The question focuses on the difference $\beta_{11} - \beta_{12}$. This is addressed directly by `Contrast 'E'`. The test statistic is 1.55 with a p-value of 0.21. There is not enough evidence from this study to suggest a difference in rate of weight loss between the two diet plans.

[5 points] (f) Women following the control (program 3) were supposed to follow their usual eating habits, under which they were presumably not losing weight, throughout the study. One issue in weight loss research is that women assigned to a control may become inspired through participation in the study to change their habits, begin following a diet plan on their own, and show a change in weight as a result. Is there evidence that this is the case here? (You need not state formal hypotheses.) From the output, provide numerical evidence (values of a test statistic and p-value) justifying your answer.

If women continued with their usual eating habits, we would expect them to exhibit no change in weight on average over the study; that is, we'd expect $\beta_{13} = 0$. We can read the $Z$ test statistic and p-value directly off the `Solutions for Fixed Effects` table as $-0.74$ and 0.46, respectively. There does not seem to be any evidence of this in the current study. Of course, this doesn't mean that it didn't happen; rather, it only means we do not have sufficient evidence to say that it did.

```
data weight; infile "weight.dat";
   input id age week weight program; run;

proc print data=weight(obs=9); run;

title "Model I";
proc mixed data=weight method=ml;
  class id program;
  model weight = week*program / solution;
  random int week / type=un subject=id;
  contrast 'A' week*program 1 0 0 week*program 0 -1 0,
               week*program 1 0 0 week*program 0 0 -1 / chisq;
  contrast 'B' week*program 1 -1 0, week*program 1 0 -1 / chisq;
  contrast 'C' week*program 1 0 0, week*program 0 1 0, week*program 0 0 1 / chisq;
  contrast 'D' week*program 1 0 0, week*program 0 -1 0 / chisq;
  contrast 'E' week*program 1 -1 0 / chisq;
run;

title "Model II";
proc mixed data=weight method=ml;
  class id program;
  model weight = week*program / solution;
  random int week / type=un subject=id group=program;
  repeated  / subject=id group=program;
run;
```

| Obs | id | age | week | weight | program |
|---|---|---|---|---|---|
| 1 | 1 | 0 | 0 | 211.3 | 1 |
| 2 | 1 | 0 | 1 | 210.1 | 1 |
| 3 | 1 | 0 | 2 | 209.2 | 1 |
| 4 | 1 | 0 | 4 | 206.1 | 1 |
| 5 | 1 | 0 | 8 | 210.1 | 1 |
| 6 | 1 | 0 | 12 | 206.8 | 1 |
| 7 | 2 | 1 | 0 | 201.9 | 1 |
| 8 | 2 | 1 | 1 | 197.1 | 1 |
| 9 | 2 | 1 | 4 | 201.5 | 1 |

Model I

The Mixed Procedure

Covariance Parameter Estimates

| Cov Parm | Subject | Estimate |
|---|---|---|
| UN(1,1) | id | 28.3760 |
| UN(2,1) | id | 0.4905 |
| UN(2,2) | id | 0.6824 |
| Residual | | 8.9744 |

Solution for Fixed Effects

| Effect | program | Estimate | Standard Error | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|---|
| Intercept | | 202.30 | 0.4644 | 149 | 435.61 | <.0001 |
| week*program | 1 | -0.7384 | 0.1299 | 442 | -5.68 | <.0001 |
| week*program | 2 | -0.5126 | 0.1262 | 442 | -4.06 | <.0001 |
| week*program | 3 | -0.09361 | 0.1269 | 442 | -0.74 | 0.4611 |

Contrasts

| Label | Num DF | Den DF | Chi-Square | F Value | Pr > ChiSq | Pr > F |
|---|---|---|---|---|---|---|
| A | 2 | 442 | 17.04 | 8.52 | 0.0002 | 0.0002 |
| B | 2 | 442 | 13.06 | 6.53 | 0.0015 | 0.0016 |
| C | 3 | 442 | 49.35 | 16.45 | <.0001 | <.0001 |
| D | 2 | 442 | 48.81 | 24.40 | <.0001 | <.0001 |
| E | 1 | 442 | 1.55 | 1.55 | 0.2126 | 0.2132 |

2. Consider the weight loss study in Problem 1. The investigators wished to carry out secondary, exploratory analyses focused on the association between age and the weight of such women when they are following their usual eating habits and between age and the "typical" rates of change at which such women lose weight under different diet programs. A popular hypothesis is that womens' weight and how women lose weight are different depending on whether they are 25 years old or younger or older than 25.

The investigators focused only on the data from "North Shore" (program 1) and "Trim-Quick" (program 2) women in these analyses and assumed the following model:

$$
\begin{aligned}
\delta_{1i} &= 1 \text{ if subject } i \text{ was assigned to "North Shore" (program 1)}, &= 0 \text{ otherwise} \\
\delta_{2i} &= 1 \text{ if subject } i \text{ was assigned to "Trim-Quick" (program 2)}, &= 0 \text{ otherwise} \\
a_i &= 0 \text{ if } i \text{ is 25 years old or less at baseline } (\leq 25) \\
&= 1 \text{ if } i \text{ is older than 25 at baseline } (> 25).
\end{aligned}
$$

$$Y_{ij} = \beta_{0i} + \beta_{1i}t_{ij} + e_{ij} \tag{3}$$

$$\beta_{0i} = \beta_{00} + \beta_{01}a_i + b_{0i}, \qquad \beta_{1i} = \beta_{11}\delta_{1i} + \beta_{11a}\delta_{1i}a_i + \beta_{12}\delta_{2i} + \beta_{12a}\delta_{2i}a_i + b_{1i} \tag{4}$$

*On page 9 you will find SAS code and selected portions of its output. Use this to answer the following.*

[5 points] (a) The first question was whether or not these data support the contention that the mean weight in the population of women who are not currently following a diet plan is associated with age group ($\leq 25$ or $> 25$). From the output, cite the numerical values of a test statistic and associated p-value appropriate for addressing this issue (you need not state formal hypotheses).

This question has to do with the state of affairs when women are not following a diet plan, so prior to starting their assigned plans. The mean weight of women of age $a_i$ at time 0 is $\beta_{00} + \beta_{01}a_i$, and we are interested in whether or not $\beta_{01} = 0$. A Wald statistic and p-value can be read off the `Solution for Fixed Effects` table and are equal to $-10.18$ and $< 0.0001$, respectively. There is strong evidence that mean weight is different depending on age group among women not following a diet plan. (The negative sign on the estimate and statistic suggests that older women weigh less on average.)

[5 points] (b) Give a numerical estimate of the difference in "typical" (mean) rate of weight change for women who are $> 25$ between the "North Shore" and "Trim-Quick" diets. Also give a standard error.

The typical mean weight change for "North Shore" (program 1) women $> 25$ is $\beta_{11} + \beta_{11a}$, and that for "Trim-Quick" (program 2) is $\beta_{12} + \beta_{12a}$. Thus, we are interested in the difference $\beta_{11} - \beta_{12} + \beta_{11a} - \beta_{12a}$. This is addressed directly by `Estimate 'C'`. The estimate and standard error are -0.2767 and 0.2038, respectively.

*Here is the model again for convenience:*

$$
\begin{array}{rcllcl}
\delta_{1i} & = & 1 \text{ if subject } i \text{ was assigned to "North Shore" (program 1),} & = & 0 \text{ otherwise} \\
\delta_{2i} & = & 1 \text{ if subject } i \text{ was assigned to "Trim-Quick" (program 2),} & = & 0 \text{ otherwise} \\
a_i & = & 0 \text{ if subject } i \text{ is 25 years old or less at baseline } (\leq 25) & & \\
 & = & 1 \text{ if subject } i \text{ is older than 25 at baseline } (> 25). & &
\end{array}
$$

$$Y_{ij} = \beta_{0i} + \beta_{1i} t_{ij} + e_{ij} \qquad (3)$$

$$\beta_{0i} = \beta_{00} + \beta_{01} a_i + b_{0i}, \qquad \beta_{1i} = \beta_{11}\delta_{1i} + \beta_{11a}\delta_{1i}a_i + \beta_{12}\delta_{2i} + \beta_{12a}\delta_{2i}a_i + b_{1i} \qquad (4)$$

[5 points] (c) Another question was whether or not, among women who follow the "North Shore" diet (program 1), the "typical" (mean) number of pounds lost per week is different between those who are $\leq 25$ years old and those who are $> 25$. From the output, cite the numerical values of a test statistic and associated p-value appropriate for addressing this issue (you need not state formal hypotheses).

The question is whether or not $\beta_{11a} = 0$. From the `Solution for Fixed Effects`, the Wald test statistic is 0.24, with a p-value of 0.81. There is no evidence to suggest that the "typical" rate of weight loss (pounds per week) for women following "North Shore" is different between the two age groups.

```
/* Delete the data for program 3 (control) */

data weight2; set weight; if program=3 then delete;  run;

proc mixed data=weight2 method=ml;
  class id program;
  model weight = age week*program age*week*program /  solution;
  random int week / type=un subject=id;
  contrast 'A' week*program 1 -1, age*week*program 1 -1 / chisq;
  contrast 'B' week*program 1 -1 / chisq;
  contrast 'C' age*week*program 1 -1 / chisq;
  contrast 'D' week*program 1 0 age*week*program -1 0 / chisq;
  contrast 'E' int 1 age 1 / chisq;
  estimate 'A' week*program 1 1 age*week*program -1 -1;
  estimate 'B' week*program 1 -1;
  estimate 'C' week*program 1 -1 age*week*program 1 -1;
  estimate 'D' week*program 1 0 age*week*program 1 0;
run;
```

The Mixed Procedure

Solution for Fixed Effects

| Effect | program | Estimate | Standard Error | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|---|
| Intercept | | 209.61 | 0.8479 | 98 | 247.21 | <.0001 |
| age | | -9.6927 | 0.9525 | 292 | -10.18 | <.0001 |
| week*program | 1 | -0.7853 | 0.2371 | 292 | -3.31 | 0.0010 |
| week*program | 2 | -0.9467 | 0.3324 | 292 | -2.85 | 0.0047 |
| age*week*program | 1 | 0.06661 | 0.2821 | 292 | 0.24 | 0.8135 |
| age*week*program | 2 | 0.5047 | 0.3587 | 292 | 1.41 | 0.1605 |

Estimates

| Label | Estimate | Standard Error | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|
| A | -2.3033 | 0.8417 | 292 | -2.74 | 0.0066 |
| B | 0.1614 | 0.4083 | 292 | 0.40 | 0.6929 |
| C | -0.2767 | 0.2038 | 292 | -1.36 | 0.1757 |
| D | -0.7187 | 0.1529 | 292 | -4.70 | <.0001 |

Contrasts

| Label | Num DF | Den DF | Chi-Square | F Value | Pr > ChiSq | Pr > F |
|---|---|---|---|---|---|---|
| A | 2 | 292 | 2.00 | 1.00 | 0.3682 | 0.3694 |
| B | 1 | 292 | 0.16 | 0.16 | 0.6926 | 0.6929 |
| C | 1 | 292 | 0.92 | 0.92 | 0.3370 | 0.3378 |
| D | 1 | 292 | 2.92 | 2.92 | 0.0872 | 0.0883 |
| E | 1 | 292 | 212062 | 212062 | <.0001 | <.0001 |

3. Consider again the weight loss study in Problem 1. *On page 11 you will find some SAS code that fits two different models (Models III and IV) to the same data as in Problem 2 ("North Shore" and "Trim-Quick" only) along with selected portions of the output. Use this to answer the following questions.*

[5 points] (a) Explain in plain English without using any symbols what Model IV assumes about variation in woman-specific "inherent" rates of weight change.

Model III assumes that "inherent" rates of weight change for women who follow the same diet and are in the same age group vary nonnegligibly about the "typical" mean rate of weight change for their diet-age group – the random effect associated with `week` captures this variation. That is, only part of the variation in woman-specific "inherent" rates of weight change is due to a systematic relationship with diet plan and age group; the rest is due to "inherent" "biological variation." On the other hand, in Model IV, these rates of change have no associated random effect to allow for "inherent" "biological variation." Thus, this model assumes that all variation in woman-specific "inherent" rates of weight change is due to a systematic relationship with diet plan and age group. The implication is that women sharing the same diet plan and age will all have the same "inherent" rate of weight change.

[5 points] (b) Based on a model that assumes "inherent" rates of weight change among women who are $< 25$ years old and assigned to "North Shore" are not identical, give a numerical expression characterizing the "inherent" rate of weight change for Subject 2 (this subject is $> 25$ years old and was assigned to "North Shore").

We want to use Model III here. The quantity we wish to "estimate" (predict) is $\beta_{11}+\beta_{11a}+b_{1i}$ for $i = 2$. From the output, we get $-0.7853 + 0.06661 + 0.3491$.

[5 points] (c) Which of Models III and IV do you prefer? Cite numerical evidence supporting your choice.

This is the problem of comparing two models with different numbers of random effects, so that the null hypothesis that the models are the same is on the boundary of the parameter space. We can compare the two models informally on the basis of AIC and BIC; from the output, Model III yields AIC = 2881.8 and BIC = 2907.9, while Model IV yields AIC = 3129.8 and BIC = 3150.7. Both measures are considerably smaller for Model III, suggesting that it may be preferred. If we wanted to do a likelihood ratio test, we would calculate the test statistic as $3113.8 - 2861.8 = 252$ and compare it to the critical value for a mixture of $\chi^2_1$ and $\chi^2_2$ distributions. The test statistic is so huge that it surely exceeds this critical value.

Thus, the evidence available seems to support Model III.

```
title "Model III";
proc mixed data=weight2 method=ml;
  class id program;
  model weight = age week*program age*week*program / solution;
  random int week / type=un subject=id solution;
run;
```

Model III

The Mixed Procedure

Covariance Parameter Estimates

| Cov Parm | Subject | Estimate |
|---|---|---|
| UN(1,1) | id | 11.1124 |
| UN(2,1) | id | 0.5331 |
| UN(2,2) | id | 0.6713 |
| Residual | | 8.6451 |

Fit Statistics

| | |
|---|---|
| -2 Log Likelihood | 2861.8 |
| AIC (smaller is better) | 2881.8 |
| BIC (smaller is better) | 2907.9 |

Solution for Fixed Effects

| Effect | program | Estimate | Standard Error | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|---|
| Intercept | | 209.61 | 0.8479 | 98 | 247.21 | <.0001 |
| age | | -9.6927 | 0.9525 | 292 | -10.18 | <.0001 |
| week*program | 1 | -0.7853 | 0.2371 | 292 | -3.31 | 0.0010 |
| week*program | 2 | -0.9467 | 0.3324 | 292 | -2.85 | 0.0047 |
| age*week*program | 1 | 0.06661 | 0.2821 | 292 | 0.24 | 0.8135 |
| age*week*program | 2 | 0.5047 | 0.3587 | 292 | 1.41 | 0.1605 |

Solution for Random Effects

| Effect | id | Estimate | Std Err Pred | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|---|
| Intercept | 1 | 0.6094 | 1.6262 | 292 | 0.37 | 0.7081 |
| week | 1 | 0.4939 | 0.3262 | 292 | 1.51 | 0.1311 |
| Intercept | 2 | 0.4987 | 1.6476 | 292 | 0.30 | 0.7623 |
| week | 2 | 0.3491 | 0.2860 | 292 | 1.22 | 0.2232 |
| Intercept | 3 | -4.7972 | 1.5643 | 292 | -3.07 | 0.0024 |
| week | 3 | -0.5238 | 0.3890 | 292 | -1.35 | 0.1792 |

```
title "Model IV";
proc mixed data=weight2 method=ml;
  class id program;
  model weight =  age week*program age*week*program / solution;
  random int / type=un subject=id  solution;
run;
```

Model IV

The Mixed Procedure

Covariance Parameter Estimates

| Cov Parm | Subject | Estimate |
|---|---|---|
| UN(1,1) | id | 24.3761 |
| Residual | | 22.6356 |

Fit Statistics

| | |
|---|---|
| -2 Log Likelihood | 3113.8 |
| AIC (smaller is better) | 3129.8 |
| BIC (smaller is better) | 3150.7 |

Solution for Fixed Effects

| Effect | program | Estimate | Standard Error | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|---|
| Intercept | | 209.60 | 1.2830 | 98 | 163.36 | <.0001 |
| age | | -9.6228 | 1.4408 | 388 | -6.68 | <.0001 |
| week*program | 1 | -0.8572 | 0.1343 | 388 | -6.38 | <.0001 |
| week*program | 2 | -0.8710 | 0.1777 | 388 | -4.90 | <.0001 |
| age*week*program | 1 | 0.1201 | 0.1612 | 388 | 0.74 | 0.4569 |
| age*week*program | 2 | 0.3971 | 0.1927 | 388 | 2.06 | 0.0400 |

Solution for Random Effects

| Effect | id | Estimate | Std Err Pred | DF | t Value | Pr > \|t\| |
|---|---|---|---|---|---|---|
| Intercept | 1 | 2.7643 | 2.0953 | 388 | 1.32 | 0.1878 |
| Intercept | 2 | 1.9481 | 2.0384 | 388 | 0.96 | 0.3398 |
| Intercept | 3 | -5.9747 | 2.0270 | 388 | -2.95 | 0.0034 |

4. A study was conducted to investigate factors associated with the control of acne in teenagers who are undergoing treatment for their acne. Data were collected on 50 such teenagers. For $j = 1, \ldots, 50$, let

$$
\begin{aligned}
Y_j &= \text{number of acne lesions on the face for teenager } j \\
g_j &= 0 \text{ if } j \text{ is a girl,} \\
&= 1 \text{ if } j \text{ is a boy} \\
t_j &= 0 \text{ if } j \text{ is using a topical medication,} \\
&= 1 \text{ if } j \text{ is using an oral medication} \\
s_j &= 0 \text{ if } j \text{ has mild to moderate acne,} \\
&= 1 \text{ if } j \text{ has severe acne.}
\end{aligned}
$$

The investigators considered the following model:

$$
E(Y_j) = \exp(\beta_0 + \beta_1 g_j + \beta_2 t_j + \beta_3 s_j) \tag{5}
$$

*On page 14, you will find the SAS code used by the investigators to fit (5) and selected portions of its output. Use this to answer the following.*

[5 points] (a) Under model (5) and any other assumptions that the investigators are apparently making in their SAS program, write down numerical estimates for the mean and variance of the number of acne lesions in the population of male teenagers who have mild to moderate acne and are using an oral medication.

The investigators are assuming that counts of lesions follow a Poisson distribution, for which the mean and the variance are equal. From the model and output, the mean number of acne lesions for subjects with $g_j = 1$, $t_j = 1$, and $s_j = 0$ is given directly by `Estimate 'B'` as 5.9516 lesions. Thus, the mean and variance are estimated as equal to this value.

[5 points] (b) The investigators wondered whether or not there is evidence to suggest that at least one of gender, type of medication, or severity of acne is associated with the mean number of acne lesions experienced by teenagers. From the output, cite numerical evidence appropriate for addressing this issue (you need not state formal hypotheses). State your conclusion regarding the strength of the evidence in support of the contention that there is such an association.

This is addressed by `Contrast 'A'`. The test statistic is 31.75 with a very small p-value. At any reasonable level of significance, we conclude that there is strong evidence that at least one of these factors is associated with the mean number of lesions.

*For convenience, here is the model again:*

$$
\begin{aligned}
Y_j &= \text{number of acne lesions on the face for teenager } j \\
g_j &= 0 \text{ if } j \text{ is a girl (female),} \\
&= 1 \text{ if } j \text{ is a boy (male)} \\
t_j &= 0 \text{ if } j \text{ is using a topical medication,} \\
&= 1 \text{ if } j \text{ is using an oral medication} \\
s_j &= 0 \text{ if } j \text{ has mild to moderate acne,} \\
&= 1 \text{ if } j \text{ has severe acne.}
\end{aligned}
$$

$$E(Y_j) = \exp(\beta_0 + \beta_1 g_j + \beta_2 t_j + \beta_3 s_j) \tag{5}$$

[5 points] (c) From the output, provide a numerical estimate of and confidence interval for the factor by which the mean number of acne lesions for teenagers with mild to moderate acne should be multiplied to obtain the mean number of lesions for teenagers with severe acne. Based on these values, is there evidence that teenagers with severe acne have more lesions on average than teenagers with mild to moderate acne?

This factor is $\exp(\beta_3)$. This quantity is estimated in `Estimate 'D'` to be 2.05, with a confidence interval of 1.50 to 2.81. The confidence interval does not contain 1.0, and its lower bound is greater than 1. This suggests that there is evidence that the mean number of lesions for teenagers with severe acne is about twice that for those with mild to moderate acne, so that teenagers with severe acne have more lesions on average.

```
data acne; infile "acne.dat";
  input id gender medicate severity lesions; run;
proc genmod data=acne;
  model lesions = gender medicate severity / dist=poisson link=log;
  contrast 'A' gender 1, medicate 1, severity 1 / wald;
  contrast 'B' int 1, gender 1, medicate 1, severity 1 / wald;
  contrast 'C' gender 1 medicate 1 severity 1 / wald;
  contrast 'D' gender 1 medicate -1, gender 1 severity -1 / wald;
  estimate 'A' gender 1 medicate 1 severity 0 /exp;
  estimate 'B' int 1 gender 1 medicate 1 severity 0 / exp;
  estimate 'C' int 1 severity 1 / exp;
  estimate 'D' int 0 severity 1 / exp;
run;
```

| Obs | id | gender | medicate | severity | lesions |
|---|---|---|---|---|---|
| 1 | 1 | 0 | 0 | 0 | 4 |
| 2 | 2 | 0 | 1 | 0 | 5 |
| 3 | 3 | 1 | 0 | 0 | 2 |
| 4 | 4 | 0 | 0 | 0 | 6 |
| 5 | 5 | 0 | 0 | 0 | 3 |

The GENMOD Procedure

Algorithm converged.

Analysis Of Parameter Estimates

| Parameter | DF | Estimate | Standard Error | Wald 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| Intercept | 1 | 1.0486 | 0.1315 | 0.7908 | 1.3063 | 63.57 | <.0001 |
| gender | 1 | 0.5805 | 0.1389 | 0.3082 | 0.8527 | 17.46 | <.0001 |
| medicate | 1 | 0.1546 | 0.1331 | -0.1062 | 0.4154 | 1.35 | 0.2452 |
| severity | 1 | 0.7201 | 0.1603 | 0.4059 | 1.0343 | 20.18 | <.0001 |
| Scale | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |

NOTE: The scale parameter was held fixed.

Contrast Estimate Results

| Label | Estimate | Standard Error | Alpha | Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| A | 0.7351 | 0.1901 | 0.05 | 0.3625 | 1.1076 | 14.96 | 0.0001 |
| Exp(A) | 2.0857 | 0.3965 | 0.05 | 1.4370 | 3.0272 | | |
| B | 1.7837 | 0.1169 | 0.05 | 1.5546 | 2.0127 | 232.91 | <.0001 |
| Exp(B) | 5.9516 | 0.6956 | 0.05 | 4.7332 | 7.4837 | | |
| C | 1.7687 | 0.1567 | 0.05 | 1.4615 | 2.0759 | 127.33 | <.0001 |
| Exp(C) | 5.8630 | 0.9190 | 0.05 | 4.3122 | 7.9714 | | |
| D | 0.7201 | 0.1603 | 0.05 | 0.4059 | 1.0343 | 20.18 | <.0001 |
| Exp(D) | 2.0546 | 0.3294 | 0.05 | 1.5007 | 2.8130 | | |

Contrast Results

| Contrast | DF | Chi-Square | Pr > ChiSq | Type |
|---|---|---|---|---|
| A | 3 | 31.75 | <.0001 | Wald |
| B | 4 | 682.92 | <.0001 | Wald |
| C | 1 | 29.01 | <.0001 | Wald |
| D | 2 | 7.98 | 0.0185 | Wald |

5. A study was conducted to investigate the effects of an antidepressant drug used to treat individuals who suffer from debilitating panic attacks. Panic attacks are temporary periods (on the order of 10 to 15 minutes) of intense fear and distress that can terrify the sufferer and interfere with his or her day-to-day life. A total of $m = 300$ subjects confirmed to suffer from such attacks were recruited and randomized to three groups:

   - Group 1 – low-dose antidepressant therapy (100 subjects)
   - Group 2 – high-dose antidepressant therapy (100 subjects)
   - Group 3 – placebo (100 subjects)

   Before starting his/her assigned treatment, each subject was asked whether or not s/he had suffered at least one panic attack in the previous week (0 = no, 1 = yes). This was taken as the subject's baseline response (week 0). All subjects then started on their assigned therapies. At 1, 2, 3, and 4 weeks thereafter, each subject visited the clinic and was asked to report whether or not s/he had suffered at least one attack in the previous week since the last visit (0 = no, 1 = yes). The gender of each subject (0 = female, 1 = male) was also recorded.

   The following table shows the proportions of subjects reporting suffering at least one attack in the previous week at each time point:

| Group | baseline (week 0) | week 1 | week 2 | week 3 | week 4 |
|---|---|---|---|---|---|
| 1 (low dose) | 0.70 | 0.61 | 0.65 | 0.59 | 0.54 |
| 2 (high dose) | 0.60 | 0.57 | 0.54 | 0.51 | 0.39 |
| 3 (placebo) | 0.67 | 0.59 | 0.64 | 0.66 | 0.66 |

   Let $Y_{ij}$ be the indicator of whether or not subject $i$ reported at least one panic attack, $i = 1, \ldots, 300$, in week $t_{ij} = 0, 1, 2, 3, 4$, and let

$$\begin{aligned}
\delta_{1i} &= 1 \text{ if subject } i \text{ was in Group 1 (low dose)}, &= 0 \text{ otherwise} \\
\delta_{2i} &= 1 \text{ if subject } i \text{ was in Group 2 (high dose)}, &= 0 \text{ otherwise} \\
\delta_{3i} &= 1 \text{ if subject } i \text{ was in Group 3 (placebo)}, &= 0 \text{ otherwise}
\end{aligned}$$

   The study team considered the following model for the probability of at least one panic attack:

$$E(Y_{ij}) = \frac{\exp(\beta_0 + \beta_1 t_{ij}\delta_{1i} + \beta_2 t_{ij}\delta_{2i} + \beta_3 t_{ij}\delta_{3i})}{1 + \exp(\beta_0 + \beta_1 t_{ij}\delta_{1i} + \beta_2 t_{ij}\delta_{2i} + \beta_3 t_{ij}\delta_{3i})} \tag{6}$$

[5 points] (a) In words, state what model (6) assumes about the pattern of change of the logarithm of the odds of having at least one panic attack in each group.

   The model assumes that the log odds is

$$\beta_0 + \beta_1 t_{ij}\delta_{1i} + \beta_2 t_{ij}\delta_{2i} + \beta_3 t_{ij}\delta_{3i}.$$

   Thus, the embedded assumption is that the log odds changes smoothly at a constant rate over time in each group, where $\beta_k$ is the change in log odds per week in group $k$.

*For convenience, here is the model again:*

$$\begin{aligned}
\delta_{1i} &= 1 \text{ if subject } i \text{ was in Group 1 (low dose)}, &= 0 \text{ otherwise}\\
\delta_{2i} &= 1 \text{ if subject } i \text{ was in Group 2 (high dose)}, &= 0 \text{ otherwise}\\
\delta_{3i} &= 1 \text{ if subject } i \text{ was in Group 3 (placebo)}, &= 0 \text{ otherwise}
\end{aligned}$$

$$E(Y_{ij}) = \frac{\exp(\beta_0 + \beta_1 t_{ij}\delta_{1i} + \beta_2 t_{ij}\delta_{2i} + \beta_3 t_{ij}\delta_{3i})}{1 + \exp(\beta_0 + \beta_1 t_{ij}\delta_{1i} + \beta_2 t_{ij}\delta_{2i} + \beta_3 t_{ij}\delta_{3i})} \tag{6}$$

*On page 18, you will find some SAS code and selected portions of its output. Use this to answer the following.*

[5 points] (b) The first question the investigators wished to address was whether or not the pattern of change of the log odds of having at least one panic attack once treatment is initiated is possibly different for at least one of three groups. From the output, cite the numerical values of a test statistic and associated p-value appropriate for addressing this issue (you need not state formal hypotheses).

The question is whether or not $\beta_1 = \beta_2 = \beta_3$. This is addressed by `Contrast 'A'`. The test statistic is 14.59 with a p-value of 0.0007. There is evidence that the pattern is different for a least one of the groups.

[5 points] (c) From the output, provide a numerical estimate of the amount by which the log odds of having at least one panic attack changes per week if high-dose antidepressant therapy is administered. Also provide the numerical value (to 4 decimal places) of an associated standard error that is valid if the assumption the investigators have made on correlations among the binary indicators of panic attacks is correct.

The log odds for the high-dose group (group 2) changes by $\beta_2$ in 1 week. Thus, the estimate is -0.2172. Assuming that the working compound symmetric correlation is correct, from the `Model-Based Standard Error Estimates` table, the standard error is 0.0460.

[5 points] (d) From the output, provide a numerical estimate for the odds ratio comparing the odds of having at least one panic attack at week 4 under low-dose therapy to the odds of having a panic attack at week 4 under high-dose therapy.

The odds of at least one panic attack at week 4 for the low-dose group is $e^{\beta_0+\beta_1(4)}$ and for the high-dose group is $e^{\beta_0+\beta_2(4)}$. The odds ratio is the quotient $e^{\beta_0+\beta_1(4)}/e^{\beta_0+\beta_2(4)} = e^{\beta_1(4)}/e^{\beta_2(4)} = e^{(\beta_1-\beta_2)(4)}$. An estimate of this quantity is given directly by `Estimate 'C'` as 1.5304. (Some of you got in indirectly from `Estimate 'A'` and `Estimate 'B'` as 0.6420/0.4195.)

*For convenience, here is the model again:*

$$\begin{array}{rclcl} \delta_{1i} & = & 1 \text{ if subject } i \text{ was in Group 1 (low dose)}, & = & 0 \text{ otherwise} \\ \delta_{2i} & = & 1 \text{ if subject } i \text{ was in Group 2 (high dose)}, & = & 0 \text{ otherwise} \\ \delta_{3i} & = & 1 \text{ if subject } i \text{ was in Group 3 (placebo)}, & = & 0 \text{ otherwise} \end{array}$$

$$E(Y_{ij}) = \frac{\exp(\beta_0 + \beta_1 t_{ij}\delta_{1i} + \beta_2 t_{ij}\delta_{2i} + \beta_3 t_{ij}\delta_{3i})}{1 + \exp(\beta_0 + \beta_1 t_{ij}\delta_{1i} + \beta_2 t_{ij}\delta_{2i} + \beta_3 t_{ij}\delta_{3i})} \qquad (6)$$

[5 points] (e) Let $g_i = 0$ if subject $i$ is female and $g_i = 1$ is male. The investigators wished to modify model (6) to allow the following:

(i) The probability of having a panic attack before starting therapy of any kind may depend on gender.

(ii) The pattern of change after week 0 for each group is of the same form as that in model (6) but may be different for males and females within each group.

Write down a modified model for $E(Y_{ij})$ that incorporates these features. Provide `class` and `model` statements that will fit your model in `proc genmod`, and give a `contrast` statement that addresses the issue of whether or not the pattern of change after week 0 differs between males and females for at least one of the three groups.

The modified model is

$$E(Y_{ij}) = \frac{\exp(\eta_{ij})}{1 + \exp(\eta_{ij})},$$

where

$$\eta_{ij} = \beta_0 + \beta_{0g} g_i + \beta_1 t_{ij}\delta_{1i} + \beta_{1g} t_{ij}\delta_{1i} g_i + \beta_2 t_{ij}\delta_{1i} + \beta_{2g} t_{ij}\delta_{1i} g_i + \beta_3 t_{ij}\delta_{1i} + \beta_{3g} t_{ij}\delta_{1i} g_i.$$

The issue in question is then whether or not at least one of $\beta_{kg}$, $k = 1, 2, 3$, is different from 0. Here is the code:

```
proc genmod descending;
  class id group;
  model attack = gender week*group week*group*gender / dist=binomial
                 link=logit;
  repeated...
  contrast 'gender' week*group*gender 1 0 0,
                    week*group*gender 0 1 0,
                    week*group*gender 0 0 1 / wald;
```

```
data panic; infile "panic.dat";
  input id attack week group gender; run;

proc print data=panic(obs=5); run;

proc genmod data=panic descending;
  class id group;
  model attack = week*group / dist=binomial link=logit;
  repeated subject=id / type=cs corrw covb modelse;
  contrast 'A' week*group 1 -1 0, week*group 1 0 -1 / wald;
  contrast 'B' week*group 1 0 0, week*group 0 1 0, week*group 0 0 1 / wald;
  contrast 'C' week*group 1 0 0, week*group 0 -1 0 / wald;
  contrast 'E' week*group 1 -1 0 / wald;
  estimate 'A' week*group 4 0 0 / exp;
  estimate 'B' week*group 0 4 0 / exp;
  estimate 'C' week*group 4 -4 0 / exp;
run;
```

| Obs | id | attack | week | group | gender |
|---|---|---|---|---|---|
| 1 | 1 | 1 | 0 | 1 | 1 |
| 2 | 1 | 0 | 1 | 1 | 1 |
| 3 | 1 | 1 | 2 | 1 | 1 |
| 4 | 1 | 0 | 3 | 1 | 1 |
| 5 | 1 | 0 | 4 | 1 | 1 |

The GENMOD Procedure

Analysis Of Initial Parameter Estimates

| Parameter | | DF | Estimate | Standard Error | Wald 95% Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|---|
| Intercept | | 1 | 0.5992 | 0.0929 | 0.4172 | 0.7813 | 41.61 | <.0001 |
| week*group | 1 | 1 | -0.0865 | 0.0481 | -0.1808 | 0.0079 | 3.23 | 0.0724 |
| week*group | 2 | 1 | -0.2347 | 0.0482 | -0.3291 | -0.1403 | 23.76 | <.0001 |
| week*group | 3 | 1 | 0.0051 | 0.0492 | -0.0914 | 0.1016 | 0.01 | 0.9169 |
| Scale | | 0 | 1.0000 | 0.0000 | 1.0000 | 1.0000 | | |

NOTE: The scale parameter was held fixed.

Working Correlation Matrix

| | Col1 | Col2 | Col3 | Col4 | Col5 |
|---|---|---|---|---|---|
| Row1 | 1.0000 | 0.3144 | 0.3144 | 0.3144 | 0.3144 |
| Row2 | 0.3144 | 1.0000 | 0.3144 | 0.3144 | 0.3144 |
| Row3 | 0.3144 | 0.3144 | 1.0000 | 0.3144 | 0.3144 |
| Row4 | 0.3144 | 0.3144 | 0.3144 | 1.0000 | 0.3144 |
| Row5 | 0.3144 | 0.3144 | 0.3144 | 0.3144 | 1.0000 |

Analysis Of GEE Parameter Estimates
Empirical Standard Error Estimates

| Parameter | Estimate | Standard Error | 95% Confidence Limits | | Z | Pr > \|Z\| |
|---|---|---|---|---|---|---|
| Intercept | 0.5996 | 0.1004 | 0.4029 | 0.7963 | 5.97 | <.0001 |
| week*group 1 | -0.1108 | 0.0481 | -0.2051 | -0.0165 | -2.30 | 0.0212 |
| week*group 2 | -0.2172 | 0.0473 | -0.3100 | -0.1244 | -4.59 | <.0001 |
| week*group 3 | 0.0123 | 0.0460 | -0.0777 | 0.1024 | 0.27 | 0.7883 |

Analysis Of GEE Parameter Estimates
Model-Based Standard Error Estimates

| Parameter | Estimate | Standard Error | 95% Confidence Limits | | Z | Pr > \|Z\| |
|---|---|---|---|---|---|---|
| Intercept | 0.5996 | 0.1022 | 0.3993 | 0.8000 | 5.87 | <.0001 |
| week*group 1 | -0.1108 | 0.0459 | -0.2008 | -0.0208 | -2.41 | 0.0158 |
| week*group 2 | -0.2172 | 0.0460 | -0.3073 | -0.1271 | -4.72 | <.0001 |
| week*group 3 | 0.0123 | 0.0475 | -0.0809 | 0.1055 | 0.26 | 0.7953 |
| Scale | 1.0000 | . | . | . | . | . |

NOTE: The scale parameter was held fixed.

The GENMOD Procedure

Contrast Estimate Results

| Label | Estimate | Standard Error | Alpha | Confidence Limits | | Chi-Square | Pr > ChiSq |
|---|---|---|---|---|---|---|---|
| A | -0.4432 | 0.1924 | 0.05 | -0.8202 | -0.0662 | 5.31 | 0.0212 |
| Exp(A) | 0.6420 | 0.1235 | 0.05 | 0.4403 | 0.9360 | | |
| B | -0.8687 | 0.1894 | 0.05 | -1.2398 | -0.4976 | 21.05 | <.0001 |
| Exp(B) | 0.4195 | 0.0794 | 0.05 | 0.2894 | 0.6080 | | |
| C | 0.4255 | 0.2460 | 0.05 | -0.0567 | 0.9077 | 2.99 | 0.0837 |
| Exp(C) | 1.5304 | 0.3765 | 0.05 | 0.9449 | 2.4785 | | |

Contrast Results for GEE Analysis

| Contrast | DF | Chi-Square | Pr > ChiSq | Type |
|---|---|---|---|---|
| A | 2 | 14.59 | 0.0007 | Wald |
| B | 3 | 25.04 | <.0001 | Wald |
| C | 2 | 23.45 | <.0001 | Wald |
| E | 1 | 2.99 | 0.0837 | Wald |