Biost 518: Applied Biostatistics II

Emerson, Winter 2006

Homework #6 Key

March 12, 2006

Written problems due at the beginning of class, Friday, March 4, 2006.

All problems relate to the SEP data set. For problem 4 it will probably be easiest if you use the dataset in "long" format as posted on the class web pages (this data set actually includes the "wide" format data as well, and that "wide" format is probably easiest for problem 1-3).

1. For this problem, restrict attention to the p60 measurement made on females, and do not use robust standard error estimates.

Table 1: Regression parameter estimates for p60 SEP peak in females.

Parameter	Right p60		Left p60		Averaged p60		Ad hoc	
	Coeff	SE	Coeff	SE	Coeff	SE	(Coeff)	(SE)
Intercept	-39.0077	24.9514	-33.8780	24.9534	-36.4429	23.4097	-36.4429	24.9524
Height	1.4156	0.3853	1.3449	0.3853	1.3803	0.3615	1.3803	0.3853
Age	1.1829	0.4514	1.0760	0.4515	1.1294	0.4235	1.1294	0.4514
Ht - Age	-0.0158	0.0071	-0.0142	0.0071	-0.0150	0.0066	-0.0150	0.0071

a. Perform an analysis of the p60 measurement on the right leg of each female. Fit terms for height, age, and the multiplicative interaction of height and age. Provide an interpretation for the intercept and each slope parameter in this model.

<u>Ans</u>: Regression parameter estimates and their estimated standard errors from the fitted model are provided in Table 1. The standard deviation of the residuals (the "Root MSE") was estimated to be 3.8378 msec. Interpretations of the parameters are:

- ***Intercept:* The estimated average time to the p60 peak when stimulating the right posterior tibial nerve in newborn (age 0) females who are 0 inches tall is -39.0 msec. (Clearly an absurd quantity scientifically. The intercept in this case is just a mathematical construct to help model the data over the range where the measurements do make sense and we do have data.)**

- ***Height slope parameter:* The estimated difference in the average time to the p60 peak on the right in newborn (age = 0) females is that taller (longer?) subjects will tend to average 1.42 msec longer for each 1 inch difference in height (body length?). (While the measurement could make sense scientifically, we clearly do not have any data on this age group in our sample. Thus we are extrapolating far outside the range of our data.)**

- ***Age slope parameter:*** **The estimated difference in the average time to the p60 peak on the right in females who are 0 inches tall is that older subjects will tend to average 1.18 msec longer for each 1 year difference in age. (No one is 0 inches tall, so, again, this is just a mathematical construct.)**

- ***Height-age interaction parameter:*** **The estimated effect of age on the relationship between the time to the p60 peak and height is measured by considering how the p60-height slope defined within age strata in females differs across those strata. From this regression model, the estimated effect of age on the relationship between time to p60 and height is such that the stratum specific p60-height slope comparing subjects of the same age is estimated to be 0.0158 msec/inch less for every 1 year difference in age between two age strata.**

b. Perform an analysis of the p60 measurement on the left leg of each female. Again, fit terms for height, age, and the multiplicative interaction of height and age. Comment on the comparability of the regression parameters and standard error estimates between this analysis and that reported in part a.

Ans: Regression parameter estimates and their estimated standard errors from the fitted model are provided in Table 1. The standard deviation of the residuals (the "Root MSE") was estimated to be 3.8381 msec. Parameter estimates are roughly the same, but not exactly so. The standard error estimates, on the other hand, are nearly identical. This is sensible, because the standard error of regression parameter estimates depends on 1) the standard deviation of the residuals (the "Root MSE"), which is nearly identical for the left and right in these data, and 2) the variance and covariance of the predictors, which is exactly identical for the left and right in this "balanced" design (i.e., we have a left and a right measurement for every individual).

c. Perform an analysis of the average of the p60 measurements made on the right and left leg of each female. Again, fit terms for height, age, and the multiplicative interaction of height and age. Comment on the comparability of the regression parameters and standard error estimates between this analysis and that reported in parts a and b. In particular, relate the standard error estimates from this model to those in parts a and b to the standard deviation of the residuals in each model and the correlation between the right and left leg measurements.

Ans: Regression parameter estimates and their estimated standard errors from the fitted model are provided in Table 1. The standard deviation of the residuals (the "Root MSE") was estimated to be 3.6006 msec. This root MSE agrees very well with that which would be predicted based on our knowledge of the variability of averages: We know that

$$p60 = \frac{(p60R + p60L)}{2} \quad \Rightarrow \quad Var(p60) = \frac{Var(p60R) + Var(p60L) + 2\rho\sqrt{Var(p60R)\,Var(p60L)}}{4}$$

So we should be able to predict the root MSE for the analysis based on the average. Now the value of the correlation between the p60R and p60L measurements should be the correlation of those measurements ADJUSTED for height, age, and the interaction. That is, we are interested in the correlation of the residuals. We have modeled any similarity between measurements on the same subject due to the height and age. The correlation of the residuals (0.76) is less extreme than the correlation between the raw measurements (0.84). As computed in the annotated Stata code, the root MSE computed for the average p60 measurements agrees exactly with what would have been predicted using the results of the separate analyses for the right and left. We get such good agreement because of the balanced design. With an unbalanced design, there might have been more differences depending upon any slight nonlinearities in the data.

Parameter estimates correspond exactly to the *"ad hoc"* estimates provided in Table 1. These *ad hoc* estimates were computed by taking the average of the parameter estimates from the model of the right measurements and the parameter estimates from the model of the left measurements. That the model of the average would produce estimates equal to the average of the estimates from the two separate models is not surprising in this setting where we 1) have a balanced data set (same distribution of predictors for the right and left measurements, and 2) are modeling the means (the average of a difference is the difference of the averages). (I note that in logistic regression or proportional hazards regression we might not observe this correspondence, even with a balanced design.)

The *"ad hoc"* standard error estimates provided in Table 1 are the square root of the average squared standard errors for the right and left. These do not agree with the standard errors of the model fit to the averaged values, primarily because of the fact that the root MSE for the model fit to the averages is less than that fit to the left and right separately.

2. For this problem, restrict attention to the p60 measurement made on males, and do not use robust standard error estimates.

Table 2: Regression parameter estimates for time to p60 on the right for males and females.

Parameter	Females p60R		Males p60R		Difference (M-F) p60R	
	Coeff	SE	Coeff	SE	Coeff	SE
Intercept	-39.0077	24.9514	39.4131	24.0205	78.4208	34.6346
Height	1.4156	0.3853	0.2384	0.3447	-1.1772	0.5169
Age	1.1829	0.4514	-0.1027	0.4302	-1.2855	0.6236
Ht - Age	-0.0158	0.0071	0.0035	0.0062	0.0193	0.0094

a. Perform an analysis of the p60 measurement on the right leg of each male. Fit terms for height, age, and the multiplicative interaction of height and age. Provide an interpretation for the intercept and each slope parameter in this model.

<u>Ans</u>: Regression parameter estimates and their estimated standard errors from the fitted model are provided in Table 2. The standard deviation of the residuals (the

"Root MSE") was estimated to be 3.9116 msec. Interpretations of the parameters are:

- ***Intercept:*** **The estimated average time to the p60 peak when stimulating the right posterior tibial nerve in newborn (age 0) males who are 0 inches tall is 39.4 msec. (Clearly an absurd quantity scientifically. The intercept in this case is just a mathematical construct to help model the data over the range where the measurements do make sense and we do have data.)**

- ***Height slope parameter:*** **The estimated difference in the average time to the p60 peak on the right in newborn (age = 0) males is that taller (longer?) subjects will tend to average 0.238 msec longer for each 1 inch difference in height (body length?). (While the measurement could make sense scientifically, we clearly do not have any data on this age group in our sample. Thus we are extrapolating far outside the range of our data.)**

- ***Age slope parameter:*** **The estimated difference in the average time to the p60 peak on the right in males who are 0 inches tall is that older subjects will tend to average 0.103 msec shorter for each 1 year difference in age. (No one is 0 inches tall, so, again, this is just a mathematical construct.)**

- ***Height-age interaction parameter:*** **The estimated effect of age on the relationship between the time to the p60 peak and height is measured by considering how the p60-height slope defined within age strata in males differs across those strata. From this regression model, the estimated effect of age on the relationship between time to p60 and height is such that the stratum specific p60-height slope comparing subjects of the same age is estimated to be 0.0035 msec/inch more for every 1 year difference in age between two age strata.**

b. Compute the difference of the regression parameter estimates found in part a of this problem and part a of problem 1. Comment on the comparability of standard error estimates and statistical significance between the results found in part a of this problem and part a of problem 1.

<u>Ans</u>**: Differences of the regression parameter estimates males minus females) and their estimated standard errors (computed as the square root of the sum of the squared standard errors estimated from the two individual models—note the males and females are independent) are provided in Table 2. Note that in each case, the difference in estimates is more than two standard errors from 0, suggesting results that are statistically significantly different from zero.**

3. For this problem, restrict attention to the p60 measurement made on both males and females, and do not use robust standard error estimates.

a. Perform an analysis of the p60 measurement on the right leg of each subject. Fit terms for height, age, sex, the two-way multiplicative interactions of height and age, height and sex, and age and sex, and the three-way multiplicative interactions of height, age, and sex. Provide an interpretation for the intercept and each slope parameter in this model.

Table 3: Regression model with two- and three-way interactions.

Parameter	Coeff	SE
Intercept	-39.0077	25.1688
Height	1.4156	0.3886
Age	1.1829	0.4553
Ht-Age Interaction	-0.0158	0.0071
Male sex	78.4208	34.6207
Height-male interaction	-1.1772	0.5171
Age-male interaction	-1.2855	0.6234
Height-age-male interaction	0.0193	0.0094

Ans: Regression parameter estimates and their estimated standard errors from the fitted model are provided in Table 3. The standard deviation of the residuals (the "Root MSE") was estimated to be 3.9116 msec. Interpretations of the parameters are:

- ***Intercept:*** **The estimated average time to the p60 peak when stimulating the right posterior tibial nerve in newborn (age 0) females who are 0 inches tall is -39.0 msec. (Clearly an absurd quantity scientifically. The intercept in this case is just a mathematical construct to help model the data over the range where the measurements do make sense and we do have data.)**

- ***Height slope parameter:*** **The estimated difference in the average time to the p60 peak on the right in newborn (age = 0) females is that taller (longer?) subjects will tend to average 1.42 msec longer for each 1 inch difference in height (body length?). (While the measurement could make sense scientifically, we clearly do not have any data on this age group in our sample. Thus we are extrapolating far outside the range of our data.)**

- ***Age slope parameter:*** **The estimated difference in the average time to the p60 peak on the right in females who are 0 inches tall is that older subjects will tend to average 1.18 msec longer for each 1 year difference in age. (No one is 0 inches tall, so, again, this is just a mathematical construct.)**

- ***Height-age interaction parameter:*** **The estimated effect of age on the relationship between the time to the p60 peak and height is measured by considering how the p60-height slope defined within age strata in females differs across those strata. From this regression model, the**

estimated effect of age on the relationship between time to p60 and height is such that the stratum specific p60-height slope comparing subjects of the same age is estimated to be 0.0158 msec/inch less for every 1 year difference in age between two age strata.

- ***Male slope parameter:*** **The estimated difference in the average time to the p60 peak when stimulating the right posterior tibial nerve in newborn (age 0) males who are 0 inches tall and the average time to the p60 peak when stimulating the right posterior tibial nerve in newborn (age 0) females who are 0 inches tall is 78.4 msec. (Clearly an absurd quantity scientifically. The parameter in this case is just a mathematical construct to help model the data over the range where the measurements do make sense and we do have data.)**

- ***Height-male interaction slope parameter:*** **The estimated difference between the "height effect" in newborn males (i.e., the difference in the average time to the p60 peak on the right in newborn (age = 0) males per 1 inch difference in height) and the "height effect" in newborn females (i.e., the difference in the average time to the p60 peak on the right in newborn (age = 0) females per 1 inch difference in height) is that the p60-height slope in newborn males is 1.18 msec/in less in newborn males than in newborn females. (While the measurement could make sense scientifically, we clearly do not have any data on this age group in our sample. Thus we are extrapolating far outside the range of our data.)**

- ***Age-male interaction slope parameter:*** **The estimated difference between the "age effect" in 0 inch tall males (i.e., the difference in the average time to the p60 peak on the right in 0 inch tall males per 1 year difference in age) and the "age effect" in 0 inch tall females (i.e., the difference in the average time to the p60 peak on the right in 0 inch tall females per 1 year difference in age) is that the p60-age slope in 0 inch tall males is 1.29 msec/year less in 0 inch tall males than in 0 inch tall females. (No one is 0 inches tall, so, again, this is just a mathematical construct.)**

- ***Height-age-male interaction parameter:*** **(Words are of little help here, but…) The estimated difference between the height-age interaction in males height-age interaction in females is 0.0193 msec/in/year.**

b. What relationships do you find between the regression parameter estimates for the results of part a of problem 1, parts a and b or problem 2, and part a of this problem?

<u>Ans</u>: As the interpretations would suggest, the parameter estimates for the intercept and the height, age, and height-age slope parameters in Table 3 agree exactly with the corresponding estimates for the females as presented in Table 2. The parameter estimates for the male slope parameter and the height-male, age-male, and height-age-male interaction slope parameters agree exactly with the difference between the males' and females' intercept and height, age, and height-age slope parameters. This

correspondence is due to fitting a sex interaction with every predictor in the models. (Note that the standard errors differ a little, because the three-way interaction model uses a pooled estimate of the standard deviation of the residuals, while the models for each sex use an estimate of the root MSE based only on that sex.

c. What can you say about the statistical significance between the difference in the height-age interaction for females and that for males?

<u>Ans</u>: Based on the "partial t test", we find a statistically significant height-age-sex interaction (P= 0.041) and thus conclude with 95% confidence that the height-age interaction is different for males and females.

d. What can you say about the statistical significance of any of the interactions you fit in part a of this problem? Compare the results of "partial" tests performed for each interaction term separately, as well as the "multiple partial" test of all interaction terms jointly.

<u>Ans</u>: Based on the "multiple partial F test" simultaneously considering the height-age, height-sex, age-sex, and height-age-sex interactions, we find that we do not have sufficient evidence to conclude that a simpler model consisting only of the height, age, and sex main effects would not adequately model the p60 data (P= 0.139). *(This seeming paradox highlights the need to identify the question you want to answer prior to doing the analysis. Given the different answers you might obtain between parts c and d of this problem, looking at both might allow people to come up with the answer they want to, thereby inflating the type I error. As detailed in the annotated Stata output, we do get consistent results between these two approaches when the influential case (ptid==140) is deleted.)*

4. For this problem, again restrict attention to the p60 measurements, but do use robust standard error estimates.

   a. Perform an analysis of the p60 measurement including data from both the right and left leg of each subject. Fit terms for height, age, sex, the two-way multiplicative interactions of height and age, height and sex, and age and sex, and the three-way multiplicative interactions of height, age, and sex. Be sure to account for the correlated p60 observations made on the same subject. Comment on how this analysis might differ from one using only the measurements made on the right leg of each subject or one using the average of measurements made on the right and left legs.

Parameter	Coeff	SE	P value	95% CI	
Intercept	-36.443	28.101	0.196	-91.789,	18.903
Height	1.380	0.428	0.001	0.538,	2.223
Age	1.129	0.443	0.011	0.257,	2.001
Ht-Age Interaction	-0.015	0.007	0.028	-0.028,	-0.002
Male sex	74.958	34.610	0.031	6.793,	143.123
Height-male interaction	-1.127	0.517	0.030	-2.145,	-0.109
Age-male interaction	-1.163	0.568	0.042	-2.282,	-0.044
Height-age-male interaction	0.018	0.009	0.041	0.001,	0.034

Ans: Table 4 contains regression parameter estimates for the model fit on the p60 measurements for both legs in both males and females. The regression parameter estimates will differ from those in problem 3, because problem 3 considered only the right legs. As noted in problem 1, when using both legs in a balanced design, we will obtain estimates that are the average of the results for the individual legs. The standard errors will tend to be smaller than the standard errors obtained for each leg separately, because we are gaining precision by using more data. The standard errors will tend to be more than those seen when modeling the average of the left and right (compare to the results for the females in problem 1), because the variability of a single measurement is more than that of the average of two measurements (the root MSE for this analysis is 3.831, while the root MSE for the analysis of the averaged right and left measurements was 3.6006).

b. Based on the above regression model, find the estimated average p60 measurement for males of age 60 and 69 inches tall. Provide a 95% confidence interval for the average p60 measurement in such a group.

Ans: We estimate that 60 year old, 69 inch tall males will average p60 measurements of 64.3 msec (95% CI 63.5 to 65.2 msec).

c. Under the assumption of normally distributed p60 measurements in each age, sex, and height group, provide a "normal range" for p60 measurements in 60 year old males who are 69 inches tall based on the 95% prediction interval.

Ans: We estimate that 95% of p60 measurements for 60 year old, 69 inch tall males will be between 56.7 and 71.9 msec.