Bios 312:
Modern Regression Analysis

Midterm Examination
March 3, 2011

Name: _____

Instructions: Please provide concise answers to all questions. Questions are of varying levels of difficult, so you may find it advantageous to skip questions you find especially difficult, and return to these questions at the end of the exam.

You are allowed three (3) pages of your own notes to assist you when taking the exam.

You may use a calculator to assist with arithmetic. When making intermediate calculations, always use at least four significant digits; report at least three significant digits.

If you come to a problem that you believe cannot be answered without making additional assumptions, clearly state the reasonable assumption that you make, and proceed.

Please adhere to the following pledge. If you are unable to truthfully sign the pledge for any reason, turn in your paper unsigned and discuss the circumstances with the instructor.

PLEDGE: On my honor, I have neither given nor received unauthorized aid on this examination

_____

This key consists of

- 12 total pages
- 175 total points
- 4 total questions, each with multiple parts
  - Question 1: 65 pts, parts (a) – (l)
  - Question 2: 30 pts, parts (a) – (d)
  - Question 3: 30 pts, parts (a) - (c)
  - Question 4: 50 pts, parts (a) - (g)

Grading infrormation:

Every student made an error on question 3, part b, so the exam was considered to be out of 170 rather than 175 points.

Grade distribution:

Stem and leaf plot of the observed grades

```
6   | 9
7   |
8   |
9   | 1 8
10  | 0 2 7
11  | 0 3 3 4
12  |
13  | 1 1 7 9
14  | 1 4
15  | 0 3 9
16  |

Total Points: 170
Max: 159
Median: 114
Mean: 121
```

Question 1 (65 points): Suppose that we are interested in the association between albumin, height, and current smoking history. The following is a summary of a linear regression analysis using robust standard erros of the following variables:

- *alb*: serum albumin measured in g/l
- *lnalb*: Natural logarithm of *alb*
- *height*: height measured in cm
- *anysmoke*: any smoking history (0=no; 1=yes)

```
Summary for variables: alb height
     by categories of: anysmoke

anysmoke |        N      mean        sd       min       p25       p50       p75       max
---------+--------------------------------------------------------------------------------
       0 |      319  3.972414  .2733282       3.2       3.8         4       4.1         5
         |      321  163.7467  9.366219       141       157       162     170.5     189.5
---------+--------------------------------------------------------------------------------
       1 |      414  3.961353  .3017369         3       3.8       3.9       4.2       5.1
         |      414  167.3519   9.69052       139       160       168     174.2     190.5
---------+--------------------------------------------------------------------------------
   Total |      733  3.966166  .2895751         3       3.8       3.9       4.2       5.1
         |      735  165.7774  9.710078       139       158     165.9     173.5     190.5
--------------------------------------------------------------------------------------------


Linear regression                                      Number of obs =     733
                                                       F(  1,   731) =    0.27
                                                       Prob > F      =  0.6039
                                                       R-squared     =  0.0004
                                                       Root MSE      =  .28972

------------------------------------------------------------------------------
             |               Robust
         alb |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    anysmoke |  -.0110611   .0213093    -0.52   0.604    -.0528958    .0307735
       _cons |   3.972414   .0153003   259.63   0.000     3.942376    4.002452
------------------------------------------------------------------------------

. regress alb height, robust

Linear regression                                      Number of obs =     733
                                                       F(  1,   731) =    6.24
                                                       Prob > F      =  0.0127
                                                       R-squared     =  0.0105
                                                       Root MSE      =  .28825

------------------------------------------------------------------------------
             |               Robust
         alb |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
      height |   .0030542   .0012231     2.50   0.013     .0006529    .0054555
       _cons |   3.459824   .2027865    17.06   0.000     3.061711    3.857937
------------------------------------------------------------------------------

. regress alb anysmoke height, robust
```

```
Linear regression                                      Number of obs =     733
                                                       F(  2,   730) =    3.44
                                                       Prob > F      =  0.0324
                                                       R-squared     =  0.0120
                                                       Root MSE      =  .28823

------------------------------------------------------------------------------
             |               Robust
         alb |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    anysmoke |  -.0228393   .0218508    -1.05   0.296    -.0657373    .0200587
      height |   .0032687   .0012641     2.59   0.010     .0007869    .0057504
       _cons |   3.437173   .2070915    16.60   0.000     3.030607    3.843739
------------------------------------------------------------------------------


. gen lnalb = log(alb)
. regress lnalb anysmoke height, robust

Linear regression                                      Number of obs =     733
                                                       F(  2,   730) =    3.57
                                                       Prob > F      =  0.0285
                                                       R-squared     =  0.0118
                                                       Root MSE      =  .07256

------------------------------------------------------------------------------
             |               Robust
       lnalb |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    anysmoke |  -.0062513   .0055066    -1.14   0.257    -.0170621    .0045594
      height |   .0008111   .0003091     2.62   0.009     .0002043    .0014178
       _cons |   1.244214   .0506479    24.57   0.000     1.144781    1.343647
------------------------------------------------------------------------------
```

End of Output.

1.a) Based on the regression model including only height, what is the best estimate for the mean Albumin in subjects with a height of 170 cm and are never-smokers? What is the best estimate for subjects with a height of 170 cm and are smokers? (5 points)

3.459824 + .0030542*170 = 3.979 g/l

1.b) Based on the regression model including both height and smoking history, what is the best estimate for the mean Albumin in subjects with a height of 150 cm and have never smoked? (5 points)

3.437173 + .0032687*150 = 3.927 g/l

Question 1 (cont.)

1.c) Based on the regression model including both height and smoking history, what is the best estimate for the mean Albumin in subjects with a height of 190 cm and have ever smoked? (5 points)

3.437173 + .0032687*190 – 0.0223893 = 4.035 g/l

1.d) Based on the regression model including both height and smoking history, what is the best estimate for the change in mean Albumin when comparing a never-smoking subject with a height of 175 cm to a never-smoking subject with a height of 176 cm? (5 points)

This is just the slope for the height coefficient: 0.0033

1.e) Based on the regression model including both height and smoking history, what is the best estimate for the change in mean Albumin when comparing a subject with a history of smoking and a height of 175 cm to a smoking subject with a height of 180 cm? Also, provide a 95% confidence interval for this estimate. (10 points)

Again, we are just using the height coefficient, but multiplying by 5 to get a 5 unit change. The upper and lower bounds of the CI are also multiplied by 5.
Estimate: 0.0163435
CI: [0.0039345, 0.0287520]

1.f) Based on the regression model including both height and smoking history, provide an interpretation for the intercept. What scientific use would you make of this estimate? (5 points)

The intercept is the expected value of albumin for never-smokers with a height of 0 cm. A height of 0 cm is well beyond the range of our observed data, and scientifically impossible, so there is no scientific use for the intercept in this model.

1.g) Based on the regression model including both height and smoking history, provide an interpretation for the height slope. What scientific use would you make of this estimate? (5 points)

The height slope provides an compares the expected change in albumin for two subjects with the same smoking history but differing in height by 1 cm. It provides a first order trend estimate of the association between height and albumin, holding smoking history constant.

Question 1 (cont.)

1.h) Based on the regression model including both height and smoking history, is there evidence that the slope for height is significantly different from 0? (5 points)

Yes. The confidence interval does not contain 0; the p-value is 0.009 (which is < 0.05)

1.i) Based on the regression model including both height and smoking history, provide an interpretation for the *anysmoke* slope. What scientific use would you make of this estimate? (5 points)

The anysmoke slope provides an estimate of the expected difference in albumin comparing two individuals who have the same height, but differ in their smoking history.

1.j) Based on the regression model including both height and smoking history, is there evidence that the slope for *anysmoke* is significantly different from 0? (5 points)

There is no evidence that smoking history is associated with albumin when controlling for height. The confidence interval contains the 0, and the p-value is 0.296 (which is > 0.05)

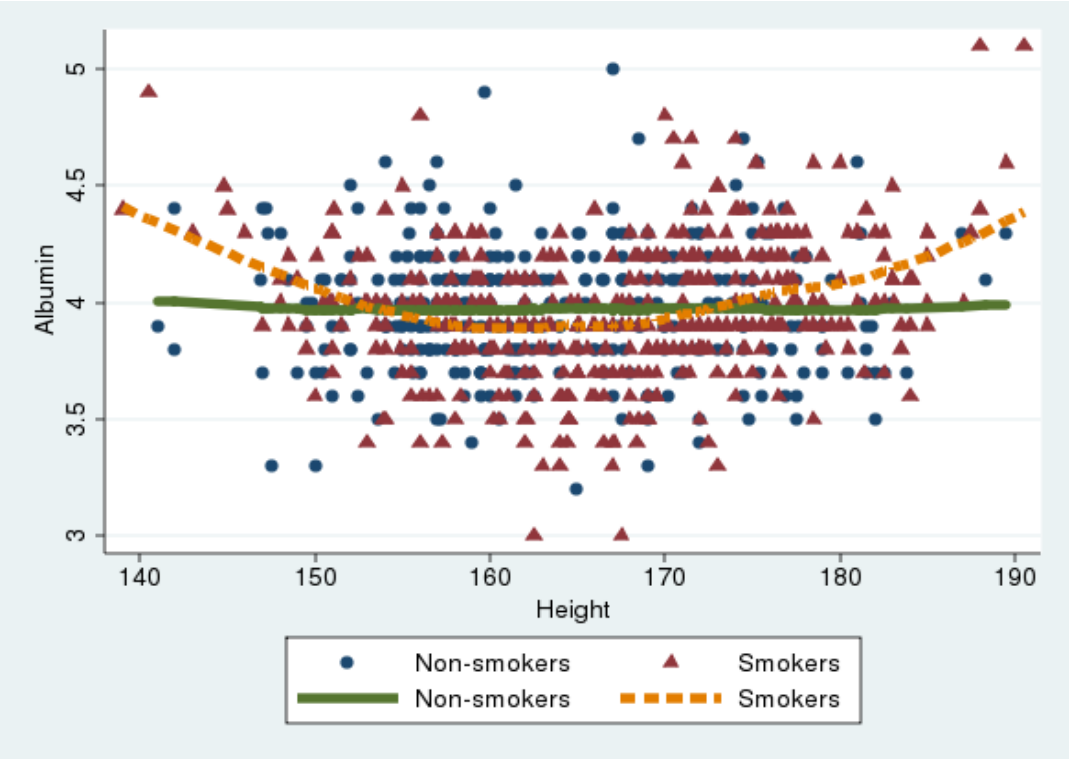
1.k) Based on the regression model including both height and smoking history, what is the best estimate of the standard deviation of Albumin in groups that are homogeneous with respect to smoking history and height? (5 points)

This is given by the root mean square error, 0.28823.

1.l) Is there any evidence that smoking history confounds the relationship between height and Albumin? What would you have to consider for smoking to be a confounder? (5 points)

For a variable to be a confounder, it must be related to both the outcome "in truth" (in the population) and associated with the predictor of interest in the sample. We cannot test these ideas statistically, but can compare the unadjusted and adjusted models to identify symptoms of confounding. In the unadjusted model, the height slope is 0.0031 and in the adjusted model it increases to 0.0033. At most, this is a symptom of weak confounding.

Question 2 (30 points): The following plot display Albumin (y-axis) byHeight (x-axis) stratified by smoking history. In a post-hoc fashion, use the additional information in this plot to evaluate the analysis from question 1 by answering the following questions



2.a) From the plot, comment on the reliability of your answers to question 1, parts (b) – (c). (5 points)

In non-smokers, there appears to be a linear (albeit very flat) association between albumin and height. To the extent that this linear association holds well, we can calculated the expected albumin in non-smokers. In smokers, we see a U-shaped relationship between albumin and height so any predictions about the expected value will be wrong. In subjects with relatively low or high height, we will underpredict the albumin levels; in subjects with average height, we will overpredict the expected albumin.

2.b) From the plot, comment on the reliability of your answers to question 1, parts (d) and (e). (5 points)

Since we are only making inference about the slopes, our estimates are still valid for describing a first-order trend in the association between height and albumin. As mentioned in 2.a, actual predictions about individual values will be incorrect for smokers and reasonable for non-smokers.

Question 2 (cont.)

2.c) From the plot, comment on the reliability of your answers to question 1, parts (h) and (j). (5 points)

Our answers should provide valid estimates of first order trends for height, and a valid measured of the adjusted association between smoking history and albumin. We used robust standard errors, which relaxes the assumption of homoskedasticity needed in classical linear regression. For smoking subjects, are model does not do a good job of estimating the U-shaped association between height and albumin. There may be an association, but it is not linear.

2.d) In problem 1, I also presented an analysis using log-transformed Albumin as the outcome with hieght and and smoking history as predictors alone. Explain how this model differs in scientific interpretation from the model with (untransformed) Albumin as the outcome. Furthermore, provide full statistical inference (parameter estimates, CIs, p-values) for the *height* and *anysmoke* predictors in this regression model (15 points)

When we use the log transformation of a continuous outcome variable in linear regression, we are now modeling the (log) geometric mean of that outcome as opposed to the arithmetic mean. Comparisons between groups are made on a multiplicative scale rather than additive scale because we compare the ratio of geometric means rather than difference of arithmetic means among groups differing by 1 unit in the predictor of interest.

To interpret the coefficients, we need to use the inverse-log function (exp) on the Stata output. Also note that $\exp(x) \approx (1 + x)$ if x is small.

Holding height constant, subjects with a history of smoking have a albumin level that is 0.6% lower than subjects without a history of smoking (95% CI: 1.7% lower to 0.5% higher). There is no evidence that smoking history is associated with albumin among subjects with the same height (p= 0.26)

Among subjects with the same smoking history, on average subjects who are 1 cm taller have a 0.1% higher albumin concentration (95% CI: 0.02% to 0.14% higher). These results are atypical of what we would expect if there was no association between albumin and height adjusting for smoking history (p = 0.009).

Question 3 (30 points): The following output represents the results from a logistic regression analysis of the risk of pre-term birth after exposure to high concentrations of disinfection byproducts (DBP) in drinking water. A case-control study was conducted in which drinking water habits were retrospectively ascertained for 50 subjects with pre-term birth (cases) and 50 subjects without preterm birth (controls). Subjects were classified as being either exposed or unexposed to high concentrations of DBP for the purpose of this analysis

We will consider the following models for p, the probability of have a pre-term birth

- $\log(p/(1-p)) = \alpha_0 + \alpha_1 * \text{exposed}$
- Cases were coded as 1, controls as 0
- Exposure was coded as an indicator variable (1=exposed, 0=not exposed)

```
Logistic regression                                   Number of obs   =        100
                                                      LR chi2(1)      =       9.24
                                                      Prob > chi2     =     0.0024
Log likelihood = -64.694635                           Pseudo R2       =     0.0667

------------------------------------------------------------------------------
    _outcome |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     exposed |   1.252763   .4225771     2.96   0.003      .424527    2.080999
       _cons |  -.5596158    .280306    -2.00   0.046    -1.109005   -.0102262
------------------------------------------------------------------------------
```

3.a) Based on the logistic regression model, what scientific conclusions can you make about the association between exposure to DBP and pre-term birth? If appropriate, include estimates of the effect size and statistical inference in your written description of the results. (10 points)

Exposure to DBP is associated with an exp(1.25) = 3.5 fold increased odds of having a pre-term birth compared to an unexposed subject. We are 95% confident that the true odds ratio lies between exp(0.4245) = 1.5 and exp(2.081) = 8.0. Since the confidence interval does not contain an odds ratio of 1, this association is not likely to be due to chance alone.

3.b) Provide an interpretation of the intercept. What scientific use can you make of this quantity? (5 points)

The intercept is the log odds of being a case (pre-term birth) in the unexposed. Since this is a case-control study, it has no valid scientific use as the probability of being a case was fixed by the study design. This estimate is heavily influence by selection probabilities.

Question 3 (cont).

3.c) Use the the regression output and the given marginal totals to fill in the missing cells of the following 2x2 contingency table. (15 points)

	Case	Control	Total
Exposed	**30**	**15**	45
Unexposed	**20**	**35**	55
Total	50	50	100

Log odds of being a case in unexposed = -0.5596
Odds of being a case in unexposed = exp(-0.5596) = 0.5714
Probability of being a case in unexposed = 0.3634
Number of cases in unexposed = 0.3634 * 55 = 20

From there, we can fill out the remainder of the table:
50 – 20 = 30 cases, exposed
45 – 30 = 15 control, exposed
50 – 15 = 55 – 20 = 35 control, unexposed

Note that you could also do a similar calculation for number of cases in the exposed by using both the intercept and the slope.

Question 4 (50 points): A scientific colleague was examining how the relationship between creatinine and age differed across the sexes. Ideally, I would want output from a linear regression of creatinine including terms for age (measured in years), an indicator of male sex (variable male=0 for females, male=1 for males), and a variable maleage= male * age. He brought to me the following output from two linear regressions of CRP on age.

```
-------------------------------------------------------------------------------
-> male = 0

Linear regression                                      Number of obs =     367
                                                       F(  1,   365) =    0.12
                                                       Prob > F      =  0.7289
                                                       R-squared     =  0.0003
                                                       Root MSE      =  2610.7

------------------------------------------------------------------------------
             |               Robust
      crt100 |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   9.089228   26.20464     0.35   0.729     -42.4418    60.62025
       _cons |   8620.363   1946.583     4.43   0.000     4792.438    12448.29
------------------------------------------------------------------------------

-------------------------------------------------------------------------------
-> male = 1

Linear regression                                      Number of obs =     366
                                                       F(  1,   364) =    5.01
                                                       Prob > F      =  0.0258
                                                       R-squared     =  0.0284
                                                       Root MSE      =  2784.6

------------------------------------------------------------------------------
             |               Robust
      crt100 |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         age |   84.21487   37.61646     2.24   0.026       10.242    158.1877
       _cons |   5693.233   2745.619     2.07   0.039     293.9654     11092.5
------------------------------------------------------------------------------
```

4.a) Suppose the researcher fit the desired model with *male, age, and maleage*. What would have been the estimated intercept in that model? (5 points)

The intercept in females: 8620

4.b) Suppose the researcher fit the desired model with *male, age, and maleage*. What would have been the estimated slope for *age*? (5 points)

The slope in females: 9.089

4.c) Suppose the researcher fit the desired model with *male, age, and maleage*. What would have been the estimated slope for *male*? (5 points)

The difference in intercepts between the two models: 5693 – 8620 = -2927

4.d) Suppose the researcher fit the desired model with *male, age, and maleage*. What would have been the estimated slope for *maleage*? (5 points)

The difference in slopes between the two models: 84.21 – 9.09 = 75.12

4.e) Is there a statistically significant difference between the *age* slope for females and the *age* slope for males? Calcuate the Z-statistic for this test, and indicate if the p-value is greater or less than 0.05. You may assume the parameter estimates from both models are independent and follow an approximately Normal distribution. [Hint: Recall that for two independent random variables X and Y, Var(X + Y) = Var(X) + Var(Y) and Var(X – Y) = Var(X) + Var(Y). $Z_{1-a/2} = Z_{0.975} = 1.96$] (10 points)

Std error of the difference = (26.20^2 + 37.62^2)^.5 = 45.84
Mean difference = 84.21 – 9.09 = 75.12
Z-statistic = 75.12 / 45.84 = 1.63
Not statistically significant because the Z-stat is less than 1.96

4.f) Suppose that we really wanted to know the creatinine and age in the entire population, irrespective of gender. If we assume that 50% of the sample is male (and 50% female), create an estimate of the *age* slope ignoring gender. Would this *age* slope likely have been significantly different from 0? [Hint: Recall that if we multiply a statistic by a constant, then we multiply the variance by a factor of the constant square. For a constant *k* and random variable X, $Var(k * X) = k^2 * Var(x)$] (10 points)

Our estimate would be the averages of the slopes = (84.21 + 9.09) / 2 = 46.65
Std error of the average = [(26.20^2 + 37.62^2) / 4]^.5 = 45.84 / 2 = 22.92
Z-statistic = 46.65 / 22.92 = 2.035
Statistically significant because the Z-stat is greater than 1.96

Note that this answer assumes that there is no (or little) confounding by gender. I would have also accepted that this was not calculatable without that assumption.

4.g) Is there any evidence that gender confounds the association between *age* and creatinine? If yes, what is that evidence. If not, what additional information would you need to evaluate symptoms of confounding in this data? (10 points)

We do not have enough information to fully answer this question. In particular, we would need the unadjusted results to determine if the adjusted and unadjusted estimates differ. The included output gives some insight into effect modification (which we tested in 4.e), but not about confounding.