Applied Biostatistics II
Final Examination Key

Name: _____ **Mailbox:** _____

Instructions: Please provide concise answers to all questions. Rambling answers touching on topics not directly relevant to the question will tend to count against you. Nearly telegraphic writing style is permissible.

The examination is closed book and closed notes. If you come to a problem that you believe cannot be answered without making additional assumptions, clearly state the reasonable assumptions that you make, and proceed.

Problems 1 through 3 pertain to the analyses of data from a hypothetical study investigating the association between sex, age, and race on serum cholesterol. Appendix 1 contains results of these analyses.

1. (10 points) Models A, B, and C each model the effects of age, race, sex, and a race-sex interaction on serum cholesterol. Which of these three models is the better one to use for such purposes? Justify your answer.

Ans: Either of models B and C are appropriate (they are in fact different parameterizations of the same model). Model A is inappropriate because it models a nominal (unordered categorical) variable continuously.

2. Using the model you identified in problem 1, answer the following questions

    a. (5 points) What is your best estimate of the expected cholesterol in a black female of age 60?

Ans: (In all parts of problem 2, I gave full credit if a student gave the estimate appropriate to the model chosen in problem 1—even if the student chose the inappropriate model A.)

A: This is answered by noting that for such a person *Age=60, Female= 1, Race= 2, Race.Female= 2:*
116.5246 + 60 * (1.3119) + 1 * (-1.6327) + 2 * (-0.8262) + 2 * (-3.2766) = 185.4003

B: This is answered by noting that for such a person *Age=60, Female= 1, Black= 1, Asian= 0, Black.Female= 1, Asian.Female= 0:*
117.731 + 60 * (1.264) + 1 * (-6.696) + 1 * (1.571) + 0 * (-1.563) + 1 * (2.812) + 0 * (-6.568) = 191.258

C: This is answered by noting that for such a person *Age=60, Female= 1, White= 0, Asian= 0, White.Female= 0, Asian.Female= 0:*
119.302 + 60 * (1.264) + 1 * (-3.885) + 0 * (-1.571) + 0 * (-3.134) + 0 * (2.812) + 0 * (-9.379) = 191.258

    b. (5 points) What is your best estimate of the expected cholesterol in a black male of age 50?

Ans: (In all parts of problem 2, I gave full credit if a student gave the estimate appropriate to the model chosen in problem 1—even if the student chose the inappropriate model A.)

A: This is answered by noting that for such a person *Age=50, Female= 0, Race= 2, Race.Female= 0:*
116.5246 + 50 * (1.3119) + 0 * (-1.6327) + 2 * (-0.8262) + 0 * (-3.2766) = 180.4672

B: This is answered by noting that for such a person *Age=50, Female= 0, Black= 1, Asian= 0, Black.Female= 0, Asian.Female= 0:*
117.731 + 50 * (1.264) + 0 * (-6.696) + 1 * (1.571) + 0 * (-1.563) + 0 * (2.812) + 0 * (-6.568) = 182.502

C: This is answered by noting that for such a person *Age=50, Female= 0, White= 0, Asian= 0, White.Female= 0, Asian.Female= 0:*
119.302 + 50 * (1.264) + 0 * (-3.885) + 0 * (-1.571) + 0 * (-3.134) + 0 * (2.812) + 0 * (-9.379) = 182.502

c. (5 points) What is your best estimate of the expected cholesterol in a black male of age 51?

Ans: (In all parts of problem 2, I gave full credit if a student gave the estimate appropriate to the model chosen in problem 1—even if the student chose the inappropriate model A.)

A: This is answered by noting that for such a person *Age=51, Female= 0, Race= 2, Race.Female= 0:*
116.5246 + 51 * (1.3119) + 0 * (-1.6327) + 2 * (-0.8262) + 0 * (-3.2766) = 181.779
(This could also have been answered by adding the slope for Age to the answer for part b:
180.4672 + 1.3119 = 181.779)

B: This is answered by noting that for such a person *Age=51, Female= 0, Black= 1, Asian= 0, Black.Female= 0, Asian.Female= 0:*
117.731 + 51 * (1.264) + 0 * (-6.696) + 1 * (1.571) + 0 * (-1.563) + 0 * (2.812) + 0 * (-6.568) = 183.766
(This could also have been answered by adding the slope for Age to the answer for part b:
182.502 + 1.264 = 1813.766)

C: This is answered by noting that for such a person *Age=51, Female= 0, White= 0, Asian= 0, White.Female= 0, Asian.Female= 0:*
119.302 + 51 * (1.264) + 0 * (-3.885) + 0 * (-1.571) + 0 * (-3.134) + 0 * (2.812) + 0 * (-9.379) = 183.766
(This could also have been answered by adding the slope for Age to the answer for part b:
182.502 + 1.264 = 1813.766)

d. (5 points) What is your best estimate of the expected difference in cholesterol when comparing a white female of age 66 to a white female of age 65?

Ans: This is just the slope for age (though you could have figured out the two predicted values and subtracted them):

A: 1.3119

B: 1.264

C: 1.264

e. (5 points) What is your best estimate of the expected difference in cholesterol when comparing an Asian male of age 60 to an Asian male of age 59?

Ans: Again, this is just the slope for age (though you could have figured out the two predicted values and subtracted them):

A: 1.3119

B: 1.264

C: 1.264

f. (5 points) What is your best estimate of the expected difference in cholesterol when comparing a white male of age 66 to a white female of age 66?

Ans: This is asking about the "sex effect" in whites, and because there is a race-sex interaction, deriving the estimates from the slopes can is a little involved, though again you could have figured out the two predicted values and subtracted them:

A: The two individuals differ by 1 unit in *Female* and 1 unit in *Race.Female,* and agree on all other modeled covearіates*:* -1.6327 – 3.2766 = -4.9093.

B: The two individuals differ by 1 unit in *Female*, and agree on all other modeled covariates: -6.696.

C: The two individuals differ by 1 unit in *Female* and 1 unit in *White.Female*, and agree on all other modeled covariates: -3.885 – 2.812 = -6.697.

g. (5 points) What is your best estimate of the expected difference in cholesterol when comparing a black male of age 66 to a white male of age 66?

Ans: This is asking about a "race effect" (whites vs. blacks) in males, and because there is a race-sex interaction, deriving the estimates from the slopes can is a little involved, though again you could have figured out the two predicted values and subtracted them:

A: The two individuals differ by 1 unit in *Race,* and agree on all other modeled covearіates*:* -0.8262.

B: The two individuals differ by 1 unit in *Black*, and agree on all other modeled covariates: 1.571.

C: The two individuals differ by -1 unit in *White*, and agree on all other modeled covariates: - (-1.571) = 1.571.

h. (5 points) What is your best estimate of the expected difference in cholesterol when comparing a black female of age 66 to a white female of age 66?

Ans: This is asking about a "race effect" (whites vs. blacks) in females, and because there is a race-sex interaction, deriving the estimates from the slopes can is a little involved, though again you could have figured out the two predicted values and subtracted them:

A: The two individuals differ by 1 unit in *Race* and 1 unit in *Race.Female,* and agree on all other modeled covearіates*:* -0.8262 + (-3.2766) = -4.1028.

B: The two individuals differ by 1 unit in *Black* and by 1 unit in *Black.Female*, and agree on all other modeled covariates: 1.571 + 2.812 = 4.383.

C: The two individuals differ by -1 unit in *White* and by -1 unit in *White.Female*, and agree on all other modeled covariates: - (-1.571) – (-2.812) = 4.383.

i. (5 points) What is your best estimate of the expected difference in cholesterol when comparing a black male of age 66 to a black female of age 66?

Ans: This is asking about the "sex effect" in blacks, and because there is a race-sex interaction, deriving the estimates from the slopes can is a little involved, though again you could have figured out the two predicted values and subtracted them:

A: The two individuals differ by 1 unit in *Female* and 2 units in *Race.Female,* and agree on all other modeled covearіates*:* -1.6327 + 2 * (– 3.2766) = -8.1859.

B: The two individuals differ by 1 unit in *Female* and 1 unit in *Black.Female*, and agree on all other modeled covariates: -6.696 + 2.812 = -3.884.

C: The two individuals differ by 1 unit in *Female*, and agree on all other modeled covariates: -3.885.

3. Using the model you identified in problem 1, answer the following questions.

    a. (5 points) Is there statistical evidence that the difference between serum cholesterol in males and females varies by race? Justify your answer, including the P value you used.

Ans: This asks if the association between cholesterol and sex is modified by race. Thus we look at a test for the race-sex interaction:

A: As there is only one covariate modeling the race-sex interaction, we look at the P value for that slope parameter: P = 0.0956. Thus we do not have enough evidence to suggest a difference among the races with respect to the association between cholesterol and sex.

B: There are two covariates modeling the race-sex interaction: *Black.Female* and *Asian.Female*. Thus we have to look at the P value from the test that these two slope parameters are simultaneously zero: P = 0.0398. Because this P value is less than 0.05, we reject the null hypothesis of no difference among the races in the association between cholesterol and sex. (Note that the P value for the race-sex interaction is statistically significant, even though neither of the individual P values are significant. This is because the individual P values are comparing blacks to whites and Asians to whites. It turns out that the biggest difference in sex effects is between blacks and Asians—see model C.)

C: There are two covariates modeling the race-sex interaction: *White.Female* and *Asian.Female*. Thus we have to look at the P value from the test that these two slope parameters are simultaneously zero: P = 0.0398. Because this P value is less than 0.05, we reject the null hypothesis of no difference among the races in the association between cholesterol and sex. (Note that if we were to look at the individual P values for the two covariates modeling the race-sex interaction, the lowest P value is 0.0141 – much lower than the true value of 0.0398. This is due to the multiple comparisons inherent in looking at pairwise comparisons of the races. With three races, there are three ways to compare them in groups of 2. If we take the lowest P value from such comparisons and judge that P value against 0.05, our type I error rate will exceed 0.05. While we could have used a Bonferroni correction by multiplying the lowest P value by 3, that would have been too conservative: 3 * 0.0141 = 0.0423. The best thing to do is use the P value simultaneously testing that all covariates modeling a race-sex interaction are zero: P= 0.0398.)

    b. (5 points) Is there statistical evidence that the difference between serum cholesterol among whites, blacks, and Asians varies by sex? Justify your answer, including the P value you used.

Ans: This asks if the association between cholesterol and race is modified by sex. Thus we look at a test for the race-sex interaction (note that if sex modifies the association between cholesterol and race, then race also modifies the association between cholesterol and sex):

A: As there is only one covariate modeling the race-sex interaction, we look at the P value for that slope parameter: P = 0.0956. Thus we do not have enough evidence to suggest a difference between the sexes with respect to the association between cholesterol and race.

B: There are two covariates modeling the race-sex interaction: *Black.Female* and *Asian.Female*. Thus we have to look at the P value from the test that these two slope parameters are simultaneously zero: P = 0.0398. Because this P value is less than 0.05, we reject the null hypothesis of no difference between the sexes in the association between cholesterol and race. (Note that the P value for the race-sex interaction is statistically significant, even though neither of the individual P values are significant. This is because the individual P values are comparing blacks to whites and Asians to whites. It turns out that the biggest difference in sex effects is between blacks and Asians—see model C.)

C: There are two covariates modeling the race-sex interaction: *White.Female* and *Asian.Female*. Thus we have to look at the P value from the test that these two slope parameters are simultaneously zero: P = 0.0398. Because this P value is less than 0.05, we reject the null hypothesis of no difference between the sexes in the association between cholesterol and race. (Note that if we were to look at the individual P values for the two covariates modeling the race-sex interaction, the lowest P value is 0.0141 – much lower than the true value of 0.0398. This is due to the multiple comparisons inherent in looking at pairwise comparisons of the races. With three races, there are three ways to compare them in groups of 2. If we take the lowest P value from such comparisons and judge that P value against 0.05, our type I error rate will exceed 0.05. While we could have used a Bonferroni correction by multiplying the lowest P value by 3, that would have been too conservative: 3 * 0.0141 = 0.0423. The best thing to do is use the P value simultaneously testing that all covariates modeling a race-sex interaction are zero: P= 0.0398.)

c. (10 points) Is there a statistically significant difference between the answers to (f) and (i) in problem 2 above? Justify your answer, including the P value you used and how you obtained it.

Ans: This asks if the association between cholesterol and sex in whites is the same as the association between cholesterol and sex in blacks. Thus this is a more restricted question than that in part a when we use dummy variables, but not when the race-sex interaction is modeled by a single continuous variable as in model A. In the presence of the multiple covariates used to model the race-sex interaction with dummy variables, it is common (but not universal) to adjust for multiple comparisons.

A: As there is only one covariate modeling the race-sex interaction, the existence of any such interaction would argue that there is a difference between the sex effect in whites and blacks. So the P value for this question is just the P value for that slope parameter: P = 0.0956. Thus we do not have enough evidence to suggest a difference between whites and blacks with respect to the association between cholesterol and sex.

B: There are two covariates modeling the race-sex interaction: *Black.Female* and *Asian.Female*. Our current question relates only to the value of *Black.Female* in this parameterization, and thus we base our decision on that P value. We do have to consider whether we should adjust for multiple comparisons: There are three pairwise comparisons of the races that could be made. We are looking at just one of them. A Bonferroni correction would thus multiply the P value by 3 to obtain: P = 3 * .4589, so I would just write P > 0.5. Of course, if this comparison between whites and blacks was the only one that would ever have been of scientific interest, adjustment for multiple comparisons would not be necessary and P = 0.4589. In either case, we do not have enough evidence to suggest a difference between whites and blacks with respect to the association between cholesterol and sex.

C: There are two covariates modeling the race-sex interaction: *White.Female* and *Asian.Female*. Our current question relates only to the value of *White.Female* in this parameterization, and thus we base our decision on that P value. We do have to consider whether we should adjust for multiple comparisons: There are three pairwise comparisons of the races that could be made. We are looking at just one of them. A Bonferroni correction would thus multiply the P value by 3 to obtain: P = 3 * .4589, so I would just write P > 0.5. Of course, if this comparison between whites and blacks was the only one that would ever have been of scientific interest, adjustment for multiple comparisons would not be necessary and P = 0.4589. In either case, we do not have enough evidence to suggest a difference between whites and blacks with respect to the association between cholesterol and sex.

4. Appendix 2 contains results from analyses of a hypothetical randomized clinical trial comparing three doses of a new drug with respect to systolic blood pressure. Use the information contained in those results to answer the following questions. You may assume that the necessary assumptions for linear regression are valid for any assumption for which there is no direct information contained in the output. Where appropriate, please identify the regression model you used to answer each question.

   a. (5 points) Is there evidence of a statistically significant imbalance in the randomization groups with respect to sex? Justify your answer.

Ans: Using the chi squared analysis, P = 0.1353, thus we cannot reject the null hypothesis that in the population (which one?) there is no association between sex and dose.

b. (5 points) Is there evidence of confounding by sex on the effect of dose on systolic blood pressure? Justify your answer.

Ans: There is a slight trend toward a higher proportion of males among the high dose groups. There is also a trend toward men having higher blood pressure on average (see model G, which suggests that men on average have a systolic blood pressure 11.29 mm Hg higher than females across all dose groups). Thus sex is associated with our predictor of interest (dose) and our response (systolic blood pressure), and may well confound our detection of an association between average blood pressure and dose. This is further demonstrated by the fact that when we model dose continuously and do not adjust for sex, each 1 unit increase in dose is estimated to cause a 0.2739 mm Hg drop in average blood pressure. However, when we do adjust for sex, each 1 unit increase in dose is estimated to cause a 0.3975 mm Hg drop in average blood pressure. Because we are comparing means, we can use the discrepancy between an unadjusted and an adjusted analysis to detect confounding. This 50% increase in the estimated effect of the drug would seem to be of scientific importance across a 20 mg/day difference in doses. ***(Note that the lack of statistical significance in part a is completely irrelevant to this question. Statistical significance plays no role in deciding about confounding. There need not be statistical significance between the confounder and the predictor of interest, because we are interested about associations that exist in the sample; statistical significance tells us about associations that exist in the population. And there need not be statistical significance between the confounder and the response, because we may lack power to detect the association, especially if evaluated in the presence of our predictor of interest: Associations between the confounder and our predictor of interest lessen our ability to detect either association with the response. I do note that usually there will be statistically significant associations between at least one of the comparisons, i.e., either the confounder and the predictor of interest or the confounder and the response. But there are no guarantees—we too often do underpowered studies.)***

c. (5 points) Suppose you decided to model dose as dummy variables. Is there evidence of an effect of the drug on blood pressure? Justify your answer, including the model used to address the question and the P value you used to make a decision. Provide a brief interpretation for the parameters in that model.

Ans: You had two basic choices here: Not adjusted for sex, or adjusted for sex. The decision should be made prior to looking at the data. As a general rule, good scientific practice would dictate prespecifying any variables that you would adjust for. Purists would say that you only adjust for variables used in the randomization, thus the unadjusted analyses would be most appropriate. However, knowing that sex might be a strong predictor of blood pressure, but also knowing that stratified randomization is logistically more of a pain than unstratified randomization, it might have been the case that no stratification was done. In such a case, it would not be unusual to prespecify that analyses would still be done after adjustment for sex. In any case, I allowed either approach. I note that models E and F are just different parameterizations of the same unadjusted model, and that models I, J, and K are also different parameterizations of the same adjusted model. I personally prefer parameterizations that use the dose 0 group as the reference group, so I will use those two as examples.

E: The test that neither the dose 10 group nor the dose 20 group differed on average from the dose 0 group suggests that we cannot reject the null hypothesis of no effect of drug on average systolic blood pressure (P = 0.1597). In this model, the intercept estimates that the average SBP in the placebo group is 141.3 mm Hg. The slope estimates suggest that the average SBP in the dose 10 group is 0.0502 mm Hg higher than that in the placebo group, while the average SBP in the dose 20 group is 5.4788 mm Hg less than that in the placebo group.

I: After adjusting for sex, the test that neither the dose 10 group nor the dose 20 group differed on average from the dose 0 group suggests that we can reject the null hypothesis of no effect of drug on average systolic blood pressure (P = 0.0243). We thus would conclude with high confidence that the treatment does have an effect on systolic blood pressure. In this model, the intercept estimates that the average SBP for females in

the placebo group is 136.4 mm Hg. The slope estimates suggest that the average SBP for males is 12.35 mm Hg higher than that for females in the same dose group, that the average SBP in the dose 10 group is 1.185 mm Hg less than that for patients of the same sex in the placebo group, and that the average SBP in the dose 20 group is 7.95 mm Hg less than that for patients of the same sex in the placebo group.

d. (5 points) Using the analysis you used in part (c), for what dose groups is there a statistically significant difference in average blood pressures? Justify your answer, including P values.

Ans: We definitely have a multiple comparison issue here. We have three ways to compare two dose groups, thus giving ourselves three chances to declare difference among dose groups. In this setting, standard statistical practice is to adjust for multiple comparisons, which I will do by the Bonferroni comparison, i.e., by multiplying each individual P value by 3. Note that I can use the equivalent models to get all three comparisons.

E and F: Bonferroni corrected unadjusted P values are: 1) for dose 10 versus placebo we consider 3 * .9879 to suggest P > 0.50, 2) for dose 20 versus placebo we consider 3 * .0988 to suggest P = 0.2964, and 3) for dose 20 versus dose 10 we consider 3 * .0957 to suggest P= 0.2871. In no case was there a statistically significant difference between the groups.

I and J: Bonferroni corrected sex adjusted P values are: 1) for dose 10 versus placebo we consider 3 * .7009 to suggest P > 0.50, 2) for dose 20 versus placebo we consider 3 * .0116 to suggest P = 0.0348, and 3) for dose 20 versus dose 10 we consider 3 * .0297 to suggest P= 0.0891. Thus we are only highly confident that a difference exists between the dose 20 and placebo groups. We cannot be sure that dose 10 would work as well as dose 20, nor can we be sure that the dose 10 group is completely ineffective (equivalent to placebo). (*For what it is worth, I simulated this data under a linear continuous model, hence in truth every dose is at least somewhat effective.)*

e. (5 points) Suppose you decided to model dose as a continuous variable. Is there evidence of an effect of the drug on blood pressure? Justify your answer, including the model used to address the question and the P value you used to make a decision. Provide a brief interpretation for the parameters in that model.

Ans: Again you had two basic choices here: Not adjusted for sex, or adjusted for sex. And again the decision should be made prior to looking at the data. All the discussion given for part c holds here as well.

D: The test that SBP does not differ across dose groups is based on the slope parameter for dose. Based on P = 0.0987, we cannot reject the null hypothesis of no effect of drug on average systolic blood pressure. In this model, the intercept estimates that the average SBP in the placebo group is 142.2 mm Hg. The slope estimate suggests that the average SBP tends to decrease 0.2739 mm Hg for each 1 mg/day of dose.

I: After adjusting for sex, we find a statistically significant trend toward lower average SBP with increasing dose (P = 0.0117). In this model, the intercept estimates that the average SBP for females in the placebo group is 137.3 mm Hg. The slope estimates suggest that the average SBP for males is 12.35 mm Hg higher than that for females in the same dose group, and that the average SBP tends to decrease 0.3975 mm Hg for each 1 mg/day of dose relative to patients of the same sex.

f. (5 points) Using the analysis you used in part (e), for what dose groups is there a statistically significant difference in average blood pressures? Justify your answer, including P values.

Ans: If we take the linear model at face value, the finding about the change in average SBP per unit of dose extends to all dose groups. Hence, in the unadjusted analysis, we cannot be confident of a difference between any two dose groups, and in the adjusted analysis we would claim confidence in declaring differences between any two groups of the same sex that differ in dose. *(Of course, I would urge you to be extremely circumspect in presuming that a the true relationship is absolutely linear. Most often, however, we are left to decide the best dose with inadequate precision to be sure which is truly optimal.)*

g. (10 points) Which of the two analyses considered in parts (c) and (e) would you prefer? Justify your answer, briefly stating the issues that you considered in making your decision.

Ans: In order to demonstrate a treatment effect, I almost always prefer a linear continuous model for dose, unless I have good reason to suspect a U-shaped trend. Adjustment for sex certainly seems appropriate based on the *post hoc* analysis, but that decision really should be made beforehand. Likely it would have been prespecified in a real trial. Actually, it is likely that randomization would have been stratified by sex.

h. (5 points) Is there evidence of confounding by dose on the effect of sex on systolic blood pressure? Justify your answer. Explain why you might get different answers to this question and part b.

Ans: There is a slight trend toward a higher proportion of males among the high dose groups. There is also a trend toward higher doses having lower blood pressure on average (see model G). Thus dose is associated with our predictor of interest (sex) and our response (systolic blood pressure), and may well confound our detection of an association between average blood pressure and sex. This is further demonstrated by the fact that when we model dose continuously and do not adjust for dose, males are estimated to average SBP 11.29 mm Hg higher than females, but after adjusting for dose, males are estimated to average SBP 12.35 mm Hg higher than females in the same dose group. Of course, if dose is not truly associated with average SBP but sex is, then sex can confound our detection of an association between SBP and dose, while dose will not confound the detection of an association between SBP and sex. In the latter case, we would not have confounding because dose is not associated with the response. The key issue is that confounding is not symmetric.

5. Consider the problem of evaluating the prognostic value of the nadir PSA on time to relapse. Recall that variable *obstime* measured time until relapse or last follow-up, with variable *inrem* measuring whether the patient was still in remission at last follow-up. Also recall that everyone was followed a minimum of 24 months, thus we could construct a variable *relapse24* that was an indicator of relapse within 24 months. For each of the following regressions, indicate whether the analysis method would be statistically and scientifically valid. When the analysis is valid, identify the measure of association being compared.

a. A linear regression of observation time (response) on nadir PSA (predictor).

Ans: This is inappropriate, because observation time is censored. We can not in general estimate the mean time to progression in the presence of censored data.

b. A linear regression of nadir PSA (response) on an indicator of relapse within 2 years

Ans: This is valid. We are comparing the difference in mean nadir PSA between patients who did and patients who did not relapse.

c. A logistic regression of an an indicator of relapse within 2 years (response) on nadir PSA (predictor)

Ans: This is valid. We are comparing the ratio of the odds of relapse within 2 years across groups defined by nadir PSA levels.

d. A proportional hazards regression model of time to relapse as measured by *obstime* on nadir PSA (predictor)

Ans: This is valid. We are comparing the ratio of the instantaneous risk of relapse across groups defined by nadir PSA levels. *(This would tend to be my top choice to answer this question, as it makes the most efficient use of the data.)*

APPENDIX 1

A simulated observational study of the relationship between serum cholesterol and age, sex and race. The following measurements were made on 100 subjects:

age	age in years
race	coded race: 1= white, 2= black, 3= Asian
female	coded sex: 0= male, 1= female
chol	serum cholesterol (mg/dl)

From those variables, the following additional variables were computed

race.female	= race * female
white	= 1 if white (race=1); 0 otherwise
black	= 1 if black (race=2); 0 otherwise
asian	= 1 if Asian (race=3); 0 otherwise
white.female	= white * female
black.female	= black * female
asian.female	= asian * female

Presented below are:

1) Selected descriptive statistics
2) Results of selected regression analyses
3) For each regression analysis, results of selected tests of multiple parameters

Descriptive statistics

Univariate descriptives:

	msng	n	freq	%	mean	std dev	min	25%-ile	median	75%-ile	maximum
age	0	100			60.53	5.92	50.67	55.17	61.05	65.42	69.78
chol	0	100			190.91	11.35	159.60	181.89	191.29	199.27	213.13
race	0	100									
Asian			34	34%							
Black			33	33%							
White			33	33%							
sex	0	100									
Female			41	41%							
Male			59	59%							

Frequencies by race and sex:

	White	Black	Asian
Male	19	20	20
Female	14	13	14

APPENDIX 1 (cont.)

Regression models

MODEL A: chol on age, female, race and female-race interaction

```
Residual Standard Error = 7.8560,  Multiple R-Square = 0.5401
N = 100,  F-statistic = 27.8900 on 4 and 95 df, p-value = 0.0000

                coef std.err   t.stat p.value 95% CIlo 95% CIhi
  Intercept  116.5246  8.4132  13.8502  0.0000   99.822 133.2269
        age    1.3119  0.1354   9.6927  0.0000    1.043   1.5806
     female   -1.6327  4.2231  -0.3866  0.6999  -10.017   6.7513
       race   -0.8262  1.2600  -0.6557  0.5136   -3.328   1.6752
race.female   -3.2766  1.9464  -1.6835  0.0956   -7.141   0.5874
```

Selected hypothesis tests on multiple parameters from Model A

```
Test female= 0.0
     race.female= 0.0
  F-statistic = 14.3000 on 2 and 95 df, p-value = 0.0000

Test race= 0.0
     race.female= 0.0
  F-statistic = 4.0080 on 2 and 95 df, p-value = 0.0213
```

APPENDIX 1 (cont.)

MODEL B: chol on age, female, black, asian and female-black, female-asian interactions

```
Residual Standard Error = 7.4510,  Multiple R-Square = 0.5949
N = 100,  F-statistic = 22.7600 on 6 and 93 df, p-value = 0.0000
                coef std.err   t.stat p.value 95% CIlo  95% CIhi
   Intercept  117.731  7.9783  14.7564  0.0000  101.888  133.5747
         age    1.264  0.1303   9.6987  0.0000    1.005    1.5226
      female   -6.696  2.6245  -2.5515  0.0124  -11.908   -1.4846
       black    1.571  2.3908   0.6570  0.5128   -3.177    6.3184
       asian   -1.563  2.3905  -0.6539  0.5148   -6.310    3.1838
black.female    2.812  3.7803   0.7438  0.4589   -4.695   10.3186
asian.female   -6.568  3.6926  -1.7786  0.0786  -13.900    0.7653
```

Selected hypothesis tests on multiple parameters from Model B

```
Test black= 0.0
     asian= 0.0
  F-statistic = 0.8739 on 2 and 93 df, p-value = 0.4207

Test black.female= 0.0
     asian.female= 0.0
  F-statistic = 3.3390 on 2 and 93 df, p-value = 0.0398

Test female= 0.0
     black.female= 0.0
     asian.female= 0.0
  F-statistic = 11.4900 on 3 and 93 df, p-value = 0.0000

Test black= 0.0
     asian= 0.0
     black.female= 0.0
     asian.female= 0.0
  F-statistic = 5.3750 on 4 and 93 df, p-value = 0.0006
```

APPENDIX 1 (cont.)

MODEL C: chol on age, female, white, asian and female-white, female-asian interactions

```
Residual Standard Error = 7.4510,  Multiple R-Square = 0.5949
N = 100,  F-statistic = 22.7600 on 6 and 93 df, p-value = 0.0000
                coef std.err   t.stat p.value 95% CIlo 95% CIhi
   Intercept  119.302  7.8397  15.2176  0.0000  103.734  134.870
         age    1.264  0.1303   9.6987  0.0000    1.005    1.523
      female   -3.885  2.7242  -1.4260  0.1572   -9.294    1.525
       white   -1.571  2.3908  -0.6570  0.5128   -6.318    3.177
       asian   -3.134  2.3706  -1.3221  0.1894   -7.842    1.573
white.female   -2.812  3.7803  -0.7438  0.4589  -10.319    4.695
asian.female   -9.379  3.7497  -2.5013  0.0141  -16.825   -1.933
```

Selected hypothesis tests on multiple parameters from Model B

```
Test white= 0.0
     asian= 0.0
  F-statistic = 0.8739 on 2 and 93 df, p-value = 0.4207

Test white.female= 0.0
     asian.female= 0.0
  F-statistic = 3.3390 on 2 and 93 df, p-value = 0.0398

Test female= 0.0
     white.female= 0.0
     asian.female= 0.0
  F-statistic = 11.4900 on 3 and 93 df, p-value = 0.0000

Test white= 0.0
     asian= 0.0
     white.female= 0.0
     asian.female= 0.0
  F-statistic = 5.3750 on 4 and 93 df, p-value = 0.0006
```

APPENDIX 2

A simulated randomized clinical trial of a new drug to treat blood pressure. 150 subjects were randomized to one of three doses. The following measurements were made:

male	coded sex: 0= female, 1= male
dose	dose administered (mg/day)
sbp	systolic blood pressure at end of study (mm Hg)

From those variables, the following variables were computed

dose0	1 if subject in dose 0 group; 0 otherwise
dose10	1 if subject in dose 10 group; 0 otherwise
dose20	1 if subject in dose 20 group; 0 otherwise

Presented below are:

1) Selected descriptive statistics
2) Results of selected regression analyses
3) For each regression analysis, results of selected tests of multiple parameters

Descriptive statistics

Univariate descriptives:

	msng	n	freq	%	mean	std dev	min	25%-ile	median	75%-ile	maximum
sbp	0	150			139.496	16.582	103.304	128.994	137.818	150.313	192.355
sex	0	150									
Female			75	50%							
Male			75	50%							
dose	0	150									
0			50	33%							
10			50	33%							
20			50	33%							

Frequencies by sex and dose

	Dose 0	Dose 10	Dose 20
Female	30	25	20
Male	20	25	30

Chi square test for association between sex and dose:
X-square = 4, df = 2, p-value = 0.1353

APPENDIX 2 (cont.)

Regression models

MODEL D: sbp on dose

```
Residual Standard Error = 16.4900,  Multiple R-Square = 0.01832
N = 150,  F-statistic = 2.7610 on 1 and 148 df, p-value = 0.0987

              coef std.err  t.stat p.value  95% CIlo 95% CIhi
Intercept  142.2349  2.1282  66.832  0.0000  138.0293 146.4406
     dose   -0.2739  0.1649  -1.662  0.0987   -0.5997   0.0518
```

MODEL E: sbp on dose10, dose20

```
Residual Standard Error = 16.4900,  Multiple R-Square = 0.02465
N = 150,  F-statistic = 1.8570 on 2 and 147 df, p-value = 0.1597

               coef std.err   t.stat p.value 95% CIlo 95% CIhi
Intercept  141.3051   2.332  60.6010  0.0000  136.697  145.913
   dose10    0.0502   3.298   0.0152  0.9879   -6.467    6.567
   dose20   -5.4788   3.298  -1.6615  0.0988  -11.996    1.038

Test dose10= 0.0
     dose20= 0.0
  F-statistic = 1.8570 on 2 and 147 df, p-value = 0.1597
```

MODEL F: sbp on dose0, dose10

```
Residual Standard Error = 16.4900,  Multiple R-Square = 0.02465
N = 150,  F-statistic = 1.8570 on 2 and 147 df, p-value = 0.1597

            coef std.err t.stat p.value  95% CIlo 95% CIhi
Intercept 135.826   2.332 58.251  0.0000  131.2183   140.43
    dose0   5.479   3.298  1.662  0.0988   -1.0380    12.00
   dose10   5.529   3.298  1.677  0.0957   -0.9878    12.05

Test dose0= 0.0
     dose10= 0.0
  F-statistic = 1.8570 on 2 and 147 df, p-value = 0.1597
```

MODEL G: sbp on male

```
Residual Standard Error = 15.6400,  Multiple R-Square = 0.1167
N = 150,  F-statistic = 19.5600 on 1 and 148 df, p-value = 0.0000
            coef std.err t.stat p.value 95% CIlo 95% CIhi
Intercept 133.85   1.806 74.130       0  130.280   137.42
     male  11.29   2.554  4.423       0    6.248    16.34
```

APPENDIX 2 (cont.)

MODEL H: sbp on male, dose

```
Residual Standard Error = 15.3500,  Multiple R-Square = 0.1543
N = 150,  F-statistic = 13.4100 on 2 and 147 df, p-value = 0.0000

              coef std.err  t.stat p.value 95% CIlo  95% CIhi
Intercept  137.2933  2.2275  61.635  0.0000  132.891  141.6954
     male   12.3541  2.5413   4.861  0.0000    7.332   17.3762
     dose   -0.3975  0.1556  -2.554  0.0117   -0.705   -0.0899
```

MODEL I: sbp on male, dose10, dose20

```
Residual Standard Error = 15.3500,  Multiple R-Square = 0.1606
N = 150,  F-statistic = 9.3120 on 3 and 146 df, p-value = 0.0000
             coef std.err   t.stat p.value 95% CIlo 95% CIhi
Intercept  136.363   2.397  56.8989  0.0000  131.627  141.100
     male   12.354   2.540   4.8631  0.0000    7.333   17.375
   dose10   -1.185   3.080  -0.3848  0.7009   -7.272    4.902
   dose20   -7.950   3.111  -2.5551  0.0116  -14.099   -1.800

Test dose10= 0.0
     dose20= 0.0
  F-statistic = 3.8150 on 2 and 146 df, p-value = 0.0243
```

MODEL J: sbp on male, dose0, dose10

```
Residual Standard Error = 15.3500,  Multiple R-Square = 0.1606
N = 150,  F-statistic = 9.3120 on 3 and 146 df, p-value = 0.0000

             coef std.err t.stat p.value 95% CIlo 95% CIhi
Intercept 128.414   2.652 48.417  0.0000 123.1721   133.66
     male  12.354   2.540  4.863  0.0000   7.3334    17.37
    dose0   7.950   3.111  2.555  0.0116   1.8005    14.10
   dose10   6.764   3.080  2.196  0.0297   0.6771    12.85

Test dose0= 0.0
     dose10= 0.0
  F-statistic = 3.8150 on 2 and 146 df, p-value = 0.0243
```

MODEL K: sbp on male, dose, dose20

```
Residual Standard Error = 15.3500,  Multiple R-Square = 0.1606
N = 150,  F-statistic = 9.3120 on 3 and 146 df, p-value = 0.0000
             coef std.err   t.stat p.value 95% CIlo  95% CIhi
Intercept  135.178   2.515  53.7520  0.0000  130.208  140.1484
     male   12.354   2.540   4.8631  0.0000    7.333   17.3747
    dose0    1.185   3.080   0.3848  0.7009   -4.902    7.2725
   dose20   -6.764   3.080  -2.1962  0.0297  -12.852   -0.6771

Test dose0= 0.0
     dose20= 0.0
  F-statistic = 3.8150 on 2 and 146 df, p-value = 0.0243
```