Biostat 518

HW 02

1/13/15

1. **Methods:** We used Lowess curves relating C-reactive protein and fibrinogen levels using Stata software ver. 13.1 to visualize the association.

**Results:** The line appears to indicate a positive association between CRP and fibrinogen levels. Though roughly linear, there may be some exponential growth at the lower end of CRP levels.



As you can see, this positive trend persists when patients with a history of cardiovascular disease are considered separately, though the slope of the line appears to be steeper for those with a diagnosis of CVD prior to enrollment in the study, as mean CRP and fibrinogen levels are higher in those with previous CVd (4.40mg/L and 334.36mg/dL, respectively) than those without (3.38mg/L and 319.57mg/dL).



11 points awarded. 7 points awarded for scatter plots/tables (3 points taken off of the total 15 as instructed for not having a table), 4 points awarded for discussion (1 point taken off for no discussion of missing data).

1. **A. Methods:** We performed a 2-sample t-test assuming equal variances with H0: µCVD=µnoCVD and HA: µCVD>µnoCVD.

**Results:** We found a history of CVD results in statistically significant (p<.0001) higher levels of blood fibrinogen, with an estimated mean difference above those without a history of CVD of 14.89mg/dL (95%CI: 10.42 - 19.35).

8 points awarded (1 point taken off for no discussion of mean values of fibrinogen for subjects with prior CVD and those without; 1 point taken off for incomplete discussion of confidence interval.)

**B. Methods:** We performed classic linear regression on fibrinogen levels by previous history of CVD.

**Results:** We obtained the same results from the t-test performed in part A; that is, the slope of the estimated best-fit first-order association between history of CVD and blood fibrinogen levels is 14.89, the same as the estimated mean difference in blood fibrinogen levels between people with and without previous CVD. The 95% CI is also the same.

8 points awarded (1 point taken off for no discussion of the intercept, 1 point taken off for no discussion of standard error; though it is implied that the standard error is the same since the 95% confidence interval is the same, the question does say to be explicit).

**C. Methods:** We performed a 2-sample t-test with unequal variances with H0: µCVD=µnoCVD and HA: µCVD>µnoCVD**.**

**Results:** We found a history of CVD results in statistically significant (p<.0001) higher levels of blood fibrinogen, with an estimated mean difference above those without a history of CVD of 14.89mg/dL (95%CI: 10.09 - 19.68).

7 points awarded (1 point taken off for no discussion of mean fibrinogen levels for the two groups. 1 point taken off for values of the confidence interval that do not match those provided in the key; this confidence interval could very well have been correct if a different method had been used, but the method used was not specified. 1 point taken off for incomplete discussion of confidence intervals.)

**D.** **Methods:** We performed classic linear regression on fibrinogen levels by previous history of CVD using robust standard error.

**Results:** We obtained the same results from the t-test performed in part C; that is, the slope of the estimated best-fit first-order association between history of CVD and blood fibrinogen levels is 14.89, the same as the estimated mean difference in blood fibrinogen levels between people with and without previous CVD. The 95% CI is also the same.

7 points awarded (1 point taken off for no discussion of the intercept, 1 point taken off for no discussion of standard error, 1 point taken off because the 95% confidence intervals are not identical, just essentially identical with large sample sizes).

**E.** The t-test allowing for unequal variance will invariably find a weaker association than a t-test assuming equal variance, since the statistic is comparing variability between groups to variability within groups.

2 points awarded. I’m happy to have the point value of this question changed if my understanding of the differences between these tests is poor, and I admit that the t-test that allows for unequal variances does provide a less extreme t-value in this case. However, I don’t think this is invariably the case, and this blanket statement does not address the specifics of the analysis at hand.

1. **A.** The estimated intercept, 319.574, is our best estimate of blood fibrinogen levels for someone with a CRP level of 0. I don’t know if that is a clinically relevant or physically possible level of CRP to have.

3 points awarded (1 point taken off because there was no specification that this was a mean fibrinogen level, 1 point taken off because of the incorrect intercept).

**B.** The estimated slope, 14.885, is our best estimate of the increase in blood fibrinogen levels for every mg/L increase in CRP levels.

3 points awarded (1 point taken off because no specification that this was a mean fibrinogen level, 1 point taken off because of the incorrect slope).

**C.** From linear regression analysis, we estimate that for each mg/L increase in CRP, blood fibrinogen levels increase an estimated 14.885mg/dl. A 95% CI suggests this estimation would not be unusual if the true value lay between 10.089 and 19.681. We reject the null hypothesis that there is no linear trend between CRP and fibrinogen with a p-value <.0001.

2 points awarded (1 point taken off for no methods/results discussion, 1 point taken off for the incorrect slope, 1 point taken off for the incorrect confidence interval).

**D.**

5 points awarded.

As far as I can tell questions 4 – 6 seem to be missing. Clearly the analyses were run, because table 1 was filled out (though the values are incorrect in the table). I would like to award:

- 4 points for the entirety of question 4 (the table was filled in, but 1 point off for incorrect answers)

- 4 points for the entirety of question 5 (the table was filled in, but 1 point off for incorrect answers)

- 4 points for the entirety of question 6 (the table was filled in, but 1 point off for incorrect answers)

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|  | **Fitted Values for Fibrinogen (mg/dL)** |
| **CRP level** | **Problem 3: mean fib mg/dl** | **Problem 4:mean fib mg/dl** | **Problem 5: geometric mean fib mg/dl** | **Problem 6: geometric mean fib mg/dl** |
| **1 mg/L** | 309.061 | 332.400 | 301.784 | 293.647 |
| **2 mg/L** | 314.303 | 369.233 | 302.800 | 294.758 |
| **3 mg/L** | 319.545 | 406.066 | 303.812 | 295.869 |
| **4 mg/L** | 324.787 | 442.899 | 304.826 | 296.980 |
| **6 mg/L** | 335.272 | 516.565 | 306.854 | 299.202 |
| **8 mg/L** | 345.756 | 590.232 | 308.882 | 301.425 |
| **9 mg/L** | 351.000 | 627.065 | 309.900 | 302.536 |
| **12 mg/L** | 366.724 | 737.564 | 312.938 | 305.870 |

For question 7, I would like to award 2.5 points (the values are generally correct in the first column, but not the last 3 columns).

 **Table 2**: Comparisons of fitted values.

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|  | **Fitted Values for Fibrinogen (mg/dL)** |
| **Comparisons across CRP level** | **Problem 3: mean fib mg/dl** | **Problem 4:mean fib mg/dl** | **Problem 5: geometric mean fib mg/dl** | **Problem 6: geometric mean fib mg/dl** |
| ***Differences*** |
| **2 mg/L – 1 mg/L** | 5.242 | 36.833 | 1.016 | 1.111 |
| **3 mg/L – 2 mg/L** | 5.242 | 36.833 | 1.012 | 1.111 |
| **4 mg/L – 1 mg/L** | 15.726 | 110.499 | 3.042 | 3.333 |
| **4 mg/L – 2 mg/L** | 10.484 | 73.666 | 2.026 | 2.222 |
| **6 mg/L – 3 mg/L** | 15.727 | 110.499 | 3.042 | 3.333 |
| **8 mg/L – 4 mg/L** | 20.969 | 147.333 | 4.056 | 4.445 |
| **9 mg/L – 6 mg/L** | 15.728 | 110.5 | 3.046 | 3.334 |
| **9 mg/L – 8 mg/L** | 5.244 | 36.833 | 1.018 | 1.111 |
| **12 mg/L – 6 mg/L** | 31.452 | 220.999 | 6.084 | 6.668 |
| ***Ratios*** |
| **2 mg/L / 1 mg/L** | 1.017 | 1.111 | 1.003 | 1.004 |
| **3 mg/L / 2 mg/L** | 1.017 | 1.100 | 1.003 | 1.004 |
| **4 mg/L / 1 mg/L** | 1.051 | 1.33 | 1.010 | 1.011 |
| **4 mg/L / 2 mg/L** | 1.033 | 1.200 | 1.010 | 1.010 |
| **6 mg/L / 3 mg/L** | 1.049 | 1.272 | 1.010 | 1.011 |
| **8 mg/L / 4 mg/L** | 1.065 | 1.333 | 1.013 | 1.015 |
| **9 mg/L / 6 mg/L** | 1.050 | 1.214 | 1.010 | 1.011 |
| **9 mg/L / 8 mg/L** | 1.015 | 1.062 | 1.003 | 1.004 |
| **12 mg/L / 6 mg/L** | 1.094 | 1.428 | 1.020 | 1.022 |

8. **A.** There were consistent differences in the fitted values when CRP and fibrinogen were analyzed as untransformed continuous variables, when only CRP was transformed (and back-transformed) to put it on a logarithmic scale, and when both CRP and fibrinogen were transformed in order to examine the geometric mean of fibrinogen.

2 points awarded for correctly identifying problem 3 and for having the correct difference of 5.25, but 3 points taken off for incorrectly identifying problems 4, 5, and 6.

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| **Comparisons across CRP level** | **Problem 3: mean fib mg/dl** | **Problem 4:mean fib mg/dl** | **Problem 5: geometric mean fib mg/dl** | **Problem 6: geometric mean fib mg/dl** |
| **2 mg/L – 1 mg/L** | **5.242** | **36.833** | 1.016 | **1.111** |
| **3 mg/L – 2 mg/L** | **5.242** | **36.833** | 1.012 | **1.111** |
| **9 mg/L – 8 mg/L** | **5.244** | **36.833** | 3.042 | **1.111** |
| **4 mg/L – 1 mg/L** | 15.726 | 110.499 | 3.042 | 3.333 |
| **6 mg/L – 3 mg/L** | 15.727 | 110.499 | 3.042 | 3.333 |
| **9 mg/L – 6 mg/L** | 15.728 | 110.5 | 3.046 | 3.334 |

**B.** There were consistent ratios in the fitted values when examining the geometric mean, regardless of whether CRP had been log-transformed or not. The untransformed data also had pretty consistent values.

2 points awarded for correctly identifying problem 5, but 2 points taken off for including problems 3 and 6, and 1 point taken off for having the wrong ratios.

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| **Comparisons across CRP level** | **Problem 3: mean fib mg/dl** | **Problem 5: geometric mean fib mg/dl** | **Problem 6: geometric mean fib mg/dl** |
| **2 mg/L / 1 mg/L** | 1.017 | **1.003** | **1.004** |
| **3 mg/L / 2 mg/L** | 1.017 | **1.003** | **1.004** |
| **9 mg/L / 8 mg/L** | 1.015 | **1.003** | **1.004** |
| **4 mg/L / 1 mg/L** | 1.051 | 1.010 | 1.011 |
| **6 mg/L / 3 mg/L** | 1.049 | 1.010 | 1.011 |
| **9 mg/L / 6 mg/L** | 1.050 | 1.010 | 1.011 |

**C.** There were no consistent differences in the fitted values when comparing groups that differ by a c-fold increase in CRP levels.

0 points awarded (incorrect answer).

**D.** There were no constant ratios in the fitted values when comparing group that differ by a c-fold increase in CRP levels.

0 points awarded. (incorrect answer).

**9.** Assuming I am using the above data and analyses to choose how to analyze future studies comparing CRP and fibrinogen, I would choose to log-transform both CRP and fibrinogen. As we talked about in class, inflammatory proteins tend to follow logarithmic scales, and I think that applies to both CRP and fibrinogen. I think that would also work well for communicating results, as you could talk about whether both are doubling at the same rate, for example.

5 points awarded.