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).



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).

**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.

**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).

**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.

**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.

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.

**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.

**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.

**D.**

|  |  |
| --- | --- |
|  | **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 |

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

|  |  |
| --- | --- |
|  | **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.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **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.

|  |  |  |  |
| --- | --- | --- | --- |
| **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.

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

**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.