

## Comments on Biostat 208 Lab #4, 1/28/10

### 1 Confounding

1. *What is the interpretation of the unadjusted and adjusted exponentiated regression coefficients for BMI, also the `lincom` and `nlcom` results?*

When the outcome is natural log-transformed,  $e^{\hat{\beta}k}$  estimates the relative change in the mean of the untransformed outcome for each  $k$ -unit increase in the predictor, and  $100(e^{\hat{\beta}k} - 1)$  estimates the corresponding percent increase. With the `eform("exp(beta)")` option in `regress`, the coefficient estimates are shown as  $e^{\hat{\beta}}$ .

Thus in the unadjusted analysis, the estimate in the `regress` output shows that each  $kg/m^2$  increase in BMI is associated with a 1.002-fold increase in creatinine (95% CI 1.001-1.004,  $p = 0.004$ ). After adjustment, a  $1 kg/m^2$  increase only predicts only 1.0015-fold higher creatinine (95% CI 1.0001-1.003,  $p = 0.036$ ).

Similarly, the first `lincom` result shows that before adjustment, that each  $5-kg/m^2$  increase in BMI is associated with 1.011-fold higher creatinine (95% CI 1.004-1.018,  $p = 0.004$ ); equivalently, the `nlcom` result shows a estimated increase in mean creatinine of about 1.1% (95% CI 0.3%-1.8%). After adjustment, the estimated effect of the  $5-kg/m^2$  increase in BMI is an 1.008-fold or 0.8% increase in creatinine.

The estimate for the effect of BMI before adjustment describes a trend in the population, but is almost surely not interpretable as causal. If the adjusted model convincingly ruled out confounding (which it almost surely does not), we might be willing to consider a causal interpretation of the adjusted estimate, specifically the hypothesis that weight gain leads to small increases in creatinine levels. To the extent that BMI reflects muscle mass, this is plausible.

### 2 Mediation

1. *Is BMI an independent predictor of TG levels? Or in other words, is there evidence that the primary predictor affects the proposed mediator?*

Each  $kg/m^2$  increase in BMI is independently associated with a 1.014-fold or 1.4% increase in TG levels ( $p < 0.0005$ ). Again not a very big effect, but highly statistically significant.

2. *Are TG levels an independent predictor of creatinine levels? What is the interpretation of the estimate for `lntg` in the `regress` output? And in the `lincom` and `nlcom` results?*

From the model including BMI, demographic and lifestyle variables, and log-TG, there is little question that TG is independently associated with creatinine ( $p < 0.0005$ ), although the effect is again not large. From the `regress` output, a 2.7-fold increase in TG (i.e., a 1-log increase) is associated with a 1.05-fold, or 5% increase in creatinine. The `lincom` and `nlcom` results show that a 25% increase in TG is associated with a 1.011-fold or 1.1% increase in creatinine.

3. *What is the interpretation of the BMI effect after adjustment for TG? Can we rule out chance as an explanation for the difference between the overall and direct effects of BMI on creatinine? What percentage of the BMI effect on creatinine is explained by TG levels?*

After adjustment for log-TG, the association of BMI with creatinine is weaker and no longer statistically significant, so there is little evidence for a “direct” effect via other pathways. Of course, TG may only be a marker for the true mediator of the BMI effect on creatinine levels. The test after `suest` ( $\chi_1^2 = 20.69, P < 0.0005$ ) rules out chance as an explanation for the difference between the overall and direct BMI effects. The estimated percentage of the BMI effect explained by TG is 44.5%.