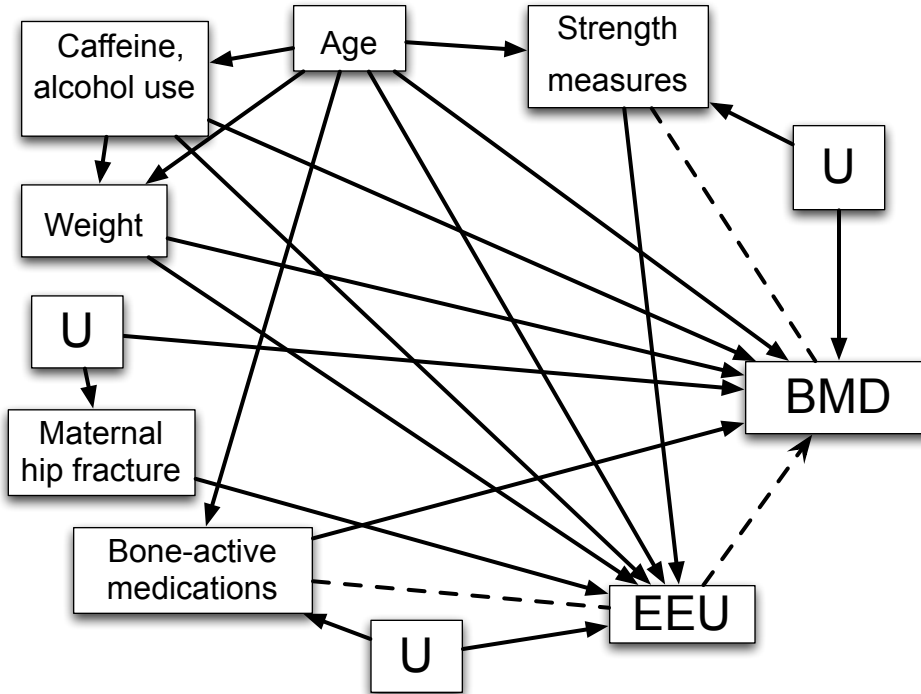


## Comments on Biostat 208 Lab #7, 2/18/10

### 1 *A priori* model

1. How did your DAG map onto your model? Here is my DAG.



In a couple of cases I have used the convention of including nodes for unmeasured confounders (U) which I think may explain associations between variables. For example, a tendency to health seeking behaviors may generate a link between use of bone active medications and EEU; similarly underlying frailty may induce a correlation between the strength measures and BMD, and genetics may link maternal hip fracture to BMD. Controlling for what we did measure on the pathway should at least reduce confounding. I included age, lifestyle variables, maternal hip fracture, strength measures, and use of bone active medications as potential confounders of medication use. And with all the arrows I have included, it would be difficult to justify removing any of the predictors from the model. More rationale below.

2. Which of the physical function variables, if any, would you include? How would you justify your decision?

I would mainly treat the physical functioning variables as confounders, on the grounds that they are markers for aging processes that drive BMD. My intuition is that the effect of EEU on physical function is probably weaker than the effect of physical function on EEU. Even if there is some mediation, controlling for the mediation would be conservative in its effect, by removing the effects of EEU by that pathway. So if we do detect an independent direct effect, the case for EEU is strengthened.

3. Should we also control for weight and history of non-spine fracture? Why or why not?

I think that the issues are about the same for EEU and weight, thus that weight should also be included in the model. Furthermore weight may be negative confounder, since it is inversely

associated with exercise and both are expected to increase BMD. But I would make a different judgment about history of non-spine fracture, since it is not associated with exercise levels and may to some extent be a result of low BMD – in short, way down the causal pathway. However, if it were associated with exercise, I would re-consider, again on the argument that we should rule out confounding as strongly as possible.

4. *How did you decide on your model, and what are the results for  $\mathbf{eeu}$ ?*

I decided that the best course would be to omit tandem stand and hip abductor strength, on the argument that we have several other measures of physical functioning, to reduce the level of missingness. I also omitted history of non-spine fracture for the reasons already cited. The model suggests that average BMD increases about  $0.0018 \text{ g/cm}^2$  (95% CI 0.00003-0.0035,  $p = 0.046$ ) for each additional 100 Kcal of exercise energy use. More later on the quantitative interpretation of the effect of  $\mathbf{eeu}$ , and it is only just borderline statistically significant, despite having 2671 observations.

5. *What are the advantages and disadvantages of selecting a model a priori?*

The clearcut advantage is that  $p$ -values and confidence intervals have their theoretical meaning; in contrast after model selection, we know that the  $p$ -values are usually too small and the CIs too narrow, but not by how much. Of course you do have to be able to motivate the model persuasively, but the determinants of BMD are reasonably well understood, so an expert could likely make good judgments about what to control for. One disadvantage is that we can end up with several variables that are apparently unimportant in the model, potentially inflating the standard error for  $\mathbf{eeu}$ , so that proponents of the benefits of exercise on BMD might criticize the model for being too large. Conversely, a more restrictive approach to *a priori* model selection could result in the omission of less well-established but non-trivial confounders.

## 2 Backwards selection model

1. *Consider the effect of modifying the  $p$ -value required for inclusion. Try out using criteria of  $p < 0.10$  and  $p < 0.05$ . How and why do the results change?*

By including tandem stand and hip abductor strength in the initial list, the number of observations is reduced to 2542. The initial backwards selection model with the liberal retention criterion of  $p < 0.20$  results in a non-significant  $p$ -value for  $\mathbf{eeu}$ , but the tighter retention criteria both result in the same final model and do solve that problem. Note that all three of these models only include 2542 observations, because the procedure only uses observations with complete data on the entire initial list of variables considered for inclusion in the model; the final count is unaffected by what gets dropped. The reduction in the standard error for  $\mathbf{eeu}$  in the smaller models is relatively minor; the bigger change is the increase in the estimate for  $\mathbf{eeu}$  from about  $0.0017 \text{ g/cm}^2$  per 100 Kcal to about 0.0020, an increase of more than 15%, suggesting that there is some residual confounding of the effect of  $\mathbf{eeu}$  by gait speed and hip abductor strength, the additional variables that get removed. So the inference about the effect of exercise is weakened at least slightly.

2. *We could modify the list of physical function variables considered for inclusion in the model to reflect concerns about the numbers of missings for tandem stand and hip abductor strength. What happens if we omit them from the list?*

This retains a larger number of observations in the analysis and gives about the same results as my *a priori* model, which also omitted tandem stand and hip abductor strength. In my view, opinion about the effect of EEU on BMD should not be strongly influenced by these minor differences in  $p$ -values, whatever their effect on the publishability of the results.

3. Interpret the estimated coefficient for EEU in the relevant units ( $g/cm^2$  for BMD and 100 Kcal/day for EEU). Suppose that walking a mile uses 150 Kcals. On average, how much increase in BMD would the model lead us to expect if a woman increased her average daily EEU by this amount? Given that average BMD is about  $0.73 g/cm^2$ , would that effect on BMD be clinically significant? How does the effect of 150 Kcal/day compare in magnitude to the effect of a 10% increase in weight or current use of estrogen?

Focusing on the estimate of  $0.0018 g/cm^2$  per 100 Kcals from my *a priori* model, an additional mile of walking per day would ideally be expected to increase BMD by  $0.0027 g/cm^2$ , or about 0.4% of the average level of  $0.73 g/cm^2$ . In contrast, a 10% increase in weight is associated with an increase of  $0.8227145 \cdot \log(1.1) = 0.078 g/cm^2$ , and current use of estrogen (`_Iestrogen_2`) is associated with an additional  $0.072 g/cm^2$ , in both cases representing increments of about 10% of the average value.

4. How much support do these data provide for the hypothesis that exercise increases BMD?

My take is that these data do provide weak support for the hypothesis, but suggest that the effect isn't particularly large. Thus only big increases in exercise energy use would be expected to have substantial effects, and it is not easy to get people to exercise. Nonetheless, we do see some independent effect after working hard to rule out confounding. In any case, increasing exercise is almost always good advice.