2007 Summer Epi/Biostat Summer Institute
Multi-level Models
Homework **Solution**

In this exercise you will be asked to interpret some results from multi-level models.

Part I: The lunch intervention

Scientific question: Does the lunch intervention impact cognitive ability?

The data consists of 4 measures of cognitive ability including:Raven's score (ravens), arithmetic score (arithmetic), Verbal meaning (vmeaning), and total digit span score (dstotal). Also included in the data are the following variables:

Lunch intervention (trt: 0=control, 1=calorie 2=meat= 3=milk)
Baseline age (age_at_time0),
Gender (1=boy 0=girl)
Baseline head circumference (head_circ)
Socioeconomic status score (ses)
Mother's reading ability (readtest)
Mother's writing ability (writetest)
Visit number (rn = 1,2,3,4,5 for weeks 1 through 5)

There were 12 schools that participated in the study. The intervention group was randomly assigned to the school. A variable number of students participated within each school. Each child was assessed at 5 times, once per week; at each occasion, the measures of cognition were recorded.

Denote the school by the index i, the student by the index j, and the visit/week by index k.

Let Y_ijk be the raven's cognition score for visit/week k (k = 1, 2, 3, 4, 5), from subject j (j = 1, …, n_i), from school i (i =1, 2, …, 12).

First we will present some summary information from the data.

The number of children participating within each school is displayed in the table below:

```
tab schoolid

   schoolid |      Freq.     Percent        Cum.
------------+-----------------------------------
          1 |         40        7.33        7.33
          2 |         27        4.95       12.27
          3 |         59       10.81       23.08
          4 |         91       16.67       39.74
          5 |         12        2.20       41.94
          6 |         51        9.34       51.28
          7 |         43        7.88       59.16
          8 |         53        9.71       68.86
          9 |         67       12.27       81.14
         10 |         20        3.66       84.80
         11 |         42        7.69       92.49
         12 |         41        7.51      100.00
------------+-----------------------------------
      Total |        546      100.00
```

The table below displays the number of children in each of the intervention groups.

```
         trt |      Freq.     Percent        Cum.
------------+-----------------------------------
    control |        127       23.26       23.26
    calorie |        146       26.74       50.00
       meat |        131       23.99       73.99
       milk |        142       26.01      100.00
------------+-----------------------------------
      Total |        546      100.00
```

The distribution of students by school and intervention group is displayed in the table below.

```
table schoolid trt

----------------------------------------------
          |                trt
 schoolid | control  calorie     meat     milk
----------+-----------------------------------
        1 |      40
        2 |                        27
        3 |                                 59
        4 |               91
        5 |               12
        6 |                        51
        7 |               43
        8 |                        53
        9 |      67
       10 |      20
       11 |                                 42
       12 |                                 41
----------------------------------------------
```

The mean raven's cognition scores by intervention group are displayed in the table below:

```
table trt, c(mean ravens sd ravens)

--------------------------------------
      trt | mean(ravens)    sd(ravens)
----------+---------------------------
  control |      18.4389      2.557517
  calorie |      18.1457       3.24382
     meat |      18.5301      3.041299
     milk |      17.9306      2.979153
--------------------------------------
```

1. Below you will find the results of an ordinary least squares linear regression for the raven's cognitive scores on the lunch intervention treatment. Specifically, we fit the following model:

$$\text{Ave(ravens score)} = b0 + b1*\text{calorie} + b2*\text{meat} + b3*\text{milk}$$

where the variables calorie, meat and milk are indicators of inclusion in each intervention group. Therefore, the control group is the reference and the mean score for the control group is represented by the intercept, b0. Note that Stata labels the intercept as "_cons". In one complete sentence interpret the regression coefficients that each compare the calorie, meat and milk groups to the control group, respectively.

Model for Ravens cognitive score

```
------------------------------------------------------------------------------
      ravens |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     calorie |  -.2932296   .1651898    -1.78   0.076    -.6171467    .0306875
     meat    |   .0911374   .1704044     0.53   0.593     -.243005    .4252798
     milk    |  -.5083678   .1664867    -3.05   0.002    -.8348281   -.1819076
       _cons |   18.43894   .1209374   152.47   0.000      18.2018    18.67609
------------------------------------------------------------------------------
```

The average raven's score among students at schools randomized to the control intervention is 18.4 (95% CI: 18.2 to 18.7). Students at schools randomized to receive the calorie or milk intervention had an average raven's score that was 0.3 or 0.5 points lower than those students at school randomized to the control, respectively (95% CI for the difference: -0.6 to 0.03 for calorie vs. control and -0.8 to -0.2 for milk vs. control). Student at schools randomized to receive the meat intervention had average raven's scores which were 0.1 points higher than the control group (95% CI: -0.2 to 0.4).

2. Next, we wish to fit a random intercept model for the raven's cognitive scores on the lunch intervention treatment taking into account all possible sources of variance in the data. Write out the model formula for this model. Your model should include three variance components. Be sure to include information regarding the distributions that you are assuming with variances defined. I got you started ……

   Y_ijk = b0 + b1*calorie_ijk + b2*meat_ijk + b3*milk_ijk + u_i + u_ij + e_ijk
   where u_i ~ Normal(0, tau^2), tau^2 is the heterogeneity in ravens cognitive scores across schools, u_ij ~ Normal(0, eta^2), eta^2 is the heterogeneity in ravens scores across students from the same school and e_ijk ~ Normal(0,sigma^2), sigma^2 is heterogeneity in ravens scores from the same student taken at multiple times.

3. Below you will find the results from fitting the random intercept model for the raven's cognitive score.

```
------------------------------------------------------------------------------
      ravens |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     calorie |  -.2671385   .2804876    -0.95   0.341    -.8168841    .2826071
     meat    |   .1233772   .2842285     0.43   0.664    -.4337005    .6804548
     milk    |  -.5235633   .2759191    -1.90   0.058    -1.064355    .0172282
       _cons |   18.43929    .200607    91.92   0.000      18.0461    18.83247
------------------------------------------------------------------------------
```

Variance at level 1 **This is the lowest level variance (corresponding to ijk)**

```
------------------------------------------------------------------------------
  6.5508953 (.20426682)

Variances and covariances of random effects
------------------------------------------------------------------------------
***level 2 (id) This is the second level variance (corresponding to ij)
    var(1): 2.2728217 (.22912251)
***level 3 (school) This is the highest level variance (corresponding to i)
    var(1): .02935327 (.05318119)
-----------------------------------------------------------------------------
```

i. Interpret the results (both the regression coefficients and random intercept variance).

The population average raven's score for schools receiving the control intervention is 18.4 (95% CI: 18.0 to 18.8). The population average difference in the raven's scores for schools receiving the calorie, meat or milk interventions relative to the control are -0.3 points (-0.8 to 0.3), 0.1 points (-0.4 to 0.7) and -0.5 points (-1.1 to 0.02). After adjusting for heterogeneity across schools, within schools and within children, there is only a moderately statistically significant difference in the population average raven's score comparing the milk intervention to control.

The intra-class correlation coefficient for measurements from the same student (implying the same school) is 2.27 + 0.03 / (6.55 + 2.27 + 0.03) = 0.26. The measurements from the same students are at best weakly correlated.

ii. Compare the results with those from OLS regression.

The estimated differences across the intervention groups are roughly similar (we don't expect them to be the same since we have more than one random intercept); however, the standard errors for the estimated differences are larger in the multi-level model relative to the OLS regression. We would announce a statistically significant difference between the meat and control interventions in the OLS model (p = 0.002) but not in the multi-level model (p = 0.058).

iii. What is the fraction of the variance that is due to within-subject variation?

The fraction of the total variance due to within-subject variation is 6.55 / (6.55 + 2.27 + 0.03) = 0.74 or 74 percent of the total variance is due to within-subject variability.

iv. What is the fraction of the variance that is due to within-school but between-subject variation?

The fraction of the total variance due to within-school but between-subject variation is 2.27 / (6.55 + 2.27 + 0.03) = 0.25 or 25 percent of the total variance is due to between subject variability within a school.

v. And what is the fraction of the variance that is due to between-school variation?

The fraction of total variance due to between-school variation is 0.03 / (6.55 +2.27 + 0.03) = 0.01 or 1 percent of the total variance is due to school to school variation.

vi. Based on your calculation of the fraction of the different variance components, do you think it would be appropriate to simplify the model? Describe how you would simplify the model and also describe one graph/figure/table that you could have made to support your decision.

There is only 1 percent of the total variance attributable to school to school differences; therefore, I would propose to drop the random school effect from the model. One graphical display that I could make would be the following: make side-by-side boxplots of the raven's scores across the schools (i.e. one boxplot for each school). In this figure, we may notice that the schools have different means/medians which depends on the treatment, but the spread of the data within each school is similar.

An alternative figure is to fit the OLS regression from question 1 and get the residuals. These residuals have the treatment effects removed. At this time, make side-by-side boxplots of the residuals where each boxplot represents a school. Here again you should see that the spread in the residuals across the schools is very similar.

4. We ran the same analysis as in question 3 but further adjusting for baseline age, gender, baseline head circumference, socioeconomic status and mother's reading and writing ability. How do the results change after the adjustment for these relevant variables?

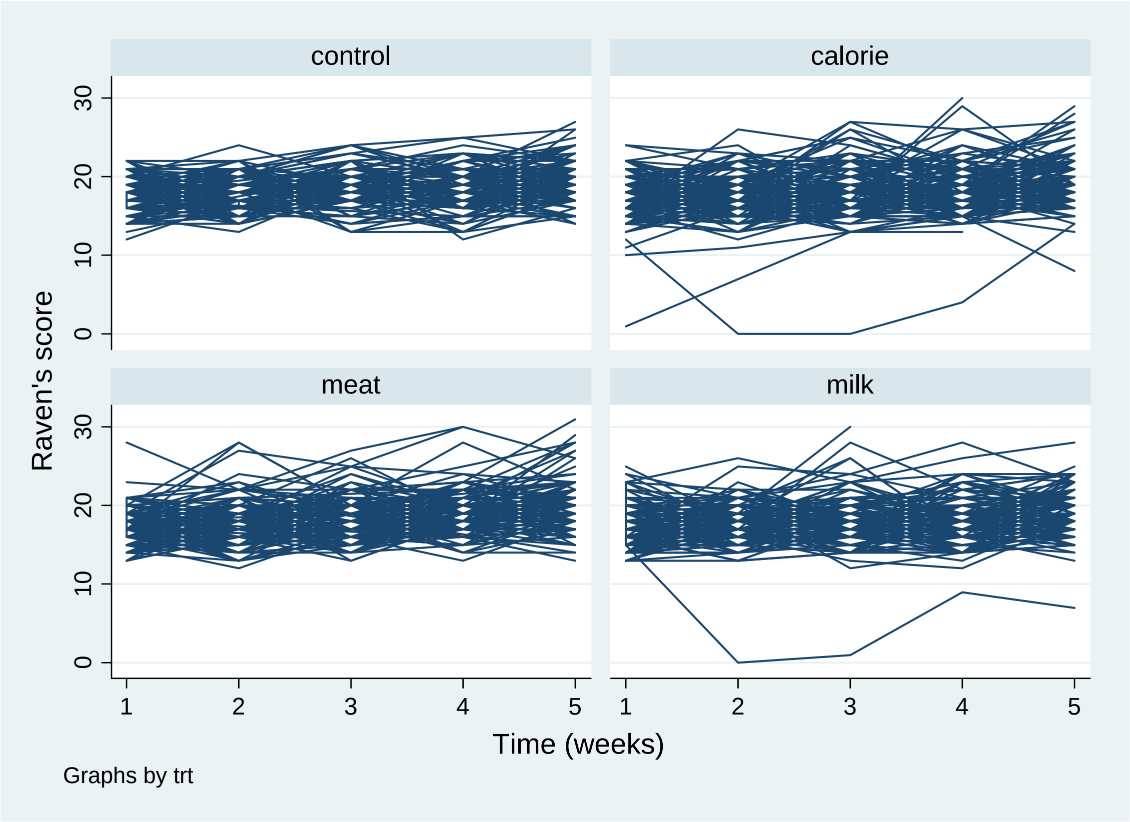
```
------------------------------------------------------------------------------
      ravens |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     calorie |  -.2770573   .2476244    -1.12   0.263    -.7623922    .2082775
     meat    |  -.0372297   .2524154    -0.15   0.883    -.5319548    .4574954
     milk    |   -.525485   .2519327    -2.09   0.037    -1.019264   -.0317059
age_at_time0 |   .1671888    .077657     2.15   0.031     .0149839    .3193938
      gender |    .301083   .1907292     1.58   0.114    -.0727393    .6749053
        ses1 |   .0043145   .0041504     1.04   0.299    -.0038202    .0124492
   head_circ |   .1899387    .066401     2.86   0.004     .0597951    .3200823
    readtest |   .0132151   .0295368     0.45   0.655    -.0446759    .0711061
   writetest |   .0242446   .0310859     0.78   0.435    -.0366826    .0851718
       _cons |   6.818578   3.340722     2.04   0.041     .2708823    13.36627
------------------------------------------------------------------------------
Variance at level 1
------------------------------------------------------------------------------
  6.3652302 (.21710862)
Variances and covariances of random effects
------------------------------------------------------------------------------
***level 2 (id)
    var(1): 1.9405232 (.22306077)
```

```
***level 3 (school)
     var(1): 1.081e-10 (.00001481)
------------------------------------------------------------------------------
```

We now estimate a decrease in raven's scores comparing the calorie, meat and milk interventions to the control group. However, the calorie and meat differences relative to control are not statistically significant. The adjustment variables are acting as qualitative confounders for the relationship between the meat vs. control association with raven's score (note that without the adjustments, we estimated a higher mean raven's score for the meat vs. control but with the adjustment we estimate a lower mean raven's score for meat vs. control. This difference either way is not statistically significant and may not be clinically relevant).

5. Next we will study the longitudinal change in raven's score over time controlling for lunch intervention as well as baseline age, gender, baseline head circumference, socioeconomic status and mother's reading and writing ability.

   The figure below displays the students' trajectories of raven's scores over time by intervention group.



NOTE: We will now ignore the index i since you established above that the degree of heterogeneity across schools was negligible. So let the index j now just count the total number of students and the index k still indicates the week of observation.

The linear random intercept model for this problem can be written out as follows:

Y_jk = b0 + b1*Time_jk + b2*calorie_j + b3*meat_j + b4*milk_j + b5*Z_j + u_j + e_jk

where Z_j contains all the adjustment variables, u_j ~ Normal(0,tau^2) and e_ij ~ Normal(0,sigma^2).

The results of fitting this model are presented below:

```
------------------------------------------------------------------------------
      ravens |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     calorie |  -.3026612   .2503153    -1.21   0.227    -.7932701    .1879477
     meat    |  -.0343622   .2562197    -0.13   0.893    -.5365436    .4678193
     milk    |  -.5552535   .2543817    -2.18   0.029    -1.053833   -.0566745
   rn (week) |   .5161691   .0367867    14.03   0.000     .4440686    .5882696
age_at_time0 |   .1676099   .0775365     2.16   0.031     .0156412    .3195786
      gender |   .2804431   .1914076     1.47   0.143    -.0947089    .6555951
        ses1 |   .0046623   .0041907     1.11   0.266    -.0035514     .012876
   head_circ |   .1970865   .0667083     2.95   0.003     .0663406    .3278324
    readtest |   .0106114   .0296023     0.36   0.720     -.047408    .0686309
   writetest |   .0303293   .0312139     0.97   0.331    -.0308488    .0915074
       _cons |   4.886603   3.340869     1.46   0.144    -1.661381    11.43459
------------------------------------------------------------------------------
Variance at level 1
------------------------------------------------------------------------------
  5.753903 (.19570873)
Variances and covariances of random effects
-----------------------------------------------------------------------------
 ***level 2 (id)
   var(1): 2.1691922 (.24278962)
------------------------------------------------------------------------------
```

i. What type of correlation structure does this linear random effects model induce for the repeated measures within each subject?

This model induces an exchangeable correlation structure among repeated measures from the same subject. I.e time is exchangeable, we don’t care about the ordering of the multiple measurements.

ii. What is the estimate of the correlation of any two raven’s scores taken from the same student?

The estimated correlation of any two raven’s scores taken from the same student is 2.17 / (5.75 + 2.17) = 0.27 indicating only a weak correlation from the repeated measurements per student.

iii. Interpret the slope for time (labeled as “rn (week)” in the Stata output).

The estimated population average slope is 0.52 (95% CI: 0.44 to 0.59) that is, we expect that the raven’s score for a given student will increase by 0.52 points per week after adjusting for intervention, age, SES and other baseline characteristics.

6. Lastly, we fit a linear random intercept and random slope on the time variable. Starting with the model given in question 5, write out the model formula where we also want to allow the slope for time to vary across students. Be sure to define the covariance between the random intercept and random slope.

   Y_jk = b0 + b1*Time_jk + b2*calorie_j + b3*meat_j + b4*milk_j + b5*Z_j + u0_j + u1_j*Time_jk + e_jk

   where Z_j contains all the adjustment variables, u0_j and u1_j are multivariate normal with mean 0 and variance tau0^2 and tau1^2 and covariance tau01, and e_ij ~ Normal(0,sigma^2).

7. The results from fitting the random intercept and slope model are presented below.

```
------------------------------------------------------------------------------
      ravens |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
     calorie |  -.2832644   .2461308    -1.15   0.250    -.7656718    .1991431
     meat    |  -.1220936   .2518864    -0.48   0.628    -.6157819    .3715947
     milk    |  -.5400549   .2504625    -2.16   0.031    -1.030952   -.0491574
   rn (week) |   .5163725   .0403634    12.79   0.000     .4372616    .5954834
age_at_time0 |   .1598898   .0772259     2.07   0.038     .0085299    .3112498
      gender |    .234042   .1901768     1.23   0.218    -.1386976    .6067816
        ses1 |   .0037936   .0041198     0.92   0.357    -.0042811    .0118683
   head_circ |   .1831787   .0660044     2.78   0.006     .0538124     .312545
    readtest |   .0135618    .029353     0.46   0.644     -.043969    .0710927
   writetest |   .0261302    .030905     0.85   0.398    -.0344425    .0867029
       _cons |    5.77438    3.32495     1.74   0.082    -.7424034    12.29116
------------------------------------------------------------------------------

Variance at level 1 This is the lowest level variance (corresponding to jk)
------------------------------------------------------------------------------
  5.2854362 (.20907831)
Variances and covariances of random effects
------------------------------------------------------------------------------
***level 2 (id)
    var(1): 2.2831446 (.60330927) This is the random intercept variance
    cov(2,1): -.2621916 (.16039095) cor(2,1): -.42572345 This is the correlation between
the subject specific random intercept and random slope.
    var(2): .16613034 (.0529639) This is the random slope variance
------------------------------------------------------------------------------
```

   i. Interpret the slope for time from this model.

The population average slope is 0.52 (95% CI: 0.44 to 0.59). This is the estimated change in raven's points per week for a student with a given random intercept and slope after adjusting for intervention, age, SES and other factors.

ii. What is the estimate of the variability in the within-in subject association between raven's scores and time? Using this information, we expect that 95% of all subjects slopes to fall within what range of the true slope?

The estimated variability in the within subject association between raven's scores and time is the variance of the random slopes; we estimate that this variance is 0.17, therefore, we expect that 95% of all students slopes to fall within +/- 2 x sqrt(0.17) points/week of the true slope. Our estimate of the true population slope is 0.52.