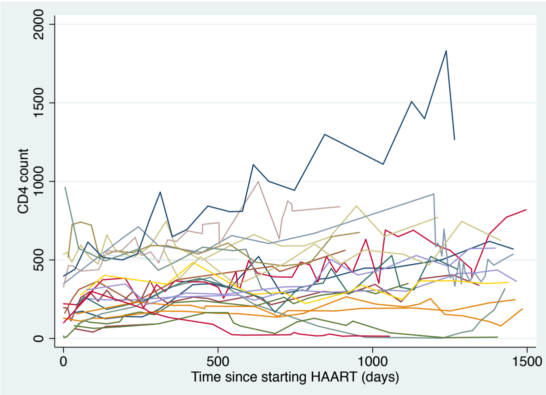

Longitudinal Data
Fall 2015

Chapter 7

Mixed, Random Effects, Random Coefficients, Multilevel, …**Models**

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Many names, some more general

- Mixed Models (most general)
- Random effects models
- Random Coefficient Models
- Hierarchical Linear Models (HLM's)
- Multilevel models (MLM's)
- Nested modeling

What's being "Mixed"?

- A mixed model has two types of effects, fixed and random.

- A fixed effect means that all levels of the variable are contained in the data and the effect is universal to all in the target population – parameters.

- A random effect means that the levels (effects) of the variable comprise random samples of the levels (effects) in the target population – random variables.

- Consider a treatment effect. Fixed, Random, Both?

Motivation for using MLM's (mixed models)

- It allows different subjects to have different responses to a treatment, risk variable, etc., thus has intuitive appeal.

- Rarely interesting, but can also provide post-estimation estimates of the random effects.

- You get the entire data-generating distribution.
  - Use the virtues of having a likelihood.
  - Can simulate data from the resulting parameter estimates
    - In contrast with other approaches that only target a specific aspect of the data-generating distribution.

Estimation of coefficients using mixed models

- As we've showed in class and homework, random effects models imply certain variance-covariance structures.

- For instance, a simple random effects model results in equal correlation (exchangeable or compound symmetry) among all observations measured on the same subject.

- We know that if the variance-covariance matrix (V) is known, then the most efficient estimate of the coefficients is weighted-least squares:

$$\hat{\beta} = (X^T W X)^{-1} X^T W \mathbf{Y}$$

where $W = V^{-1}$.

Estimation of coefficients using mixed models, cont.

- The Mixed Linear Model procedure works by:
  1. Converting the random effects model into its implied variance-covariance matrix, *V*,
  2. starting with the independent model (OLS) it gets residuals and then estimates *V* based on this model,
  3. creates weight matrix as $W = \hat{V}^{-1}$,
  4. does weighted least squares and gets residuals,
  5. repeats until convergence.

- The SE's the procedure return come from:

$$\hat{\mathrm{var}}(\hat{\beta}_{\hat{V}}) = (X^T W X)^{-1} = (X^T \hat{V}^{-1} X)^{-1}$$

Model Based inference

When deriving the inference on coefficients, $SE(\hat{\beta})$ the estimating procedure assumes that the variance-covariance model of the outcome implied by the model IS CORRECT (i.e., it's always naïve, not "robust").

The Simplest Example.

- The Model:

$$Y_{ij} = \mu + \alpha_i + e_{ij}$$

- $E(\alpha_i)=0$, $E(e_{ij})=0$, $E[\alpha_i e_{ij}]=0$.

- $Var(\alpha_i) = \sigma^2_\alpha$.

- $Var(e_{ij}) = \sigma^2_e$.

- What are the fixed and random effects in this model?

Likelihood

- Given α_i:

$$f(Y_{ij} \mid \alpha_i) = \phi\left(\frac{Y_{ij} - \alpha_i - \mu}{\sigma_e^2}\right), f(\vec{Y}_i \mid \alpha_i) = \prod_{j=1}^{n_i} \phi\left(\frac{Y_{ij} - \alpha_i - \mu}{\sigma_e^2}\right)$$

- Likelihood of observed data (for one unit) is:

$$f(\vec{Y}_i) = \int_\alpha f(\vec{Y}_i \mid \alpha) f(\alpha) d\alpha = \int_\alpha \prod_{j=1}^{n_i} \phi\left(\frac{Y_{ij} - \alpha - \mu}{\sigma_e^2}\right) \phi\left(\frac{\alpha}{\sigma_\alpha^2}\right) d\alpha$$

Random Intercepts and *Random Associations*

- The Model: $Y_{ij} = \left(\beta_0 + \beta_{0i}\right) + (\beta_1 + \beta_{1i})x_{ij} + e_{ij}$

- $E(\beta_{0i})=0$, $E(\beta_{1i})=0$, $E(e_{ij})=0$.

- $Var(\beta_{0i})= \sigma^2{}_0$, $Var(\beta^1{}_i)= \sigma^2{}_1$, $Var(e_{ij})= \sigma^2$

- $cov(\beta_{0i}, \beta_{1i})= \sigma_{12}$, $cov(\beta_{0i}, e_{ij})=0$, $cov(\beta_{1i}, e_{ij})=0$.

- What are the fixed and random effects in this model?

Reminder of our GEE analysis: Association of Baseline Covariate (Age) on CD4 count.

- Binary age (X_{ij}) = 0 (<40) or 1 (>40)
- Fit simple linear model:

$$E[Y_{ij} \mid X_{ij} = x_i] = \beta_0 + \beta_1 x_i$$

- Compare results of Models A-D

	Naive	**Robust**
Unweighted OLS	A	B
Weighted LS	C	D

Summary of Results of Association of Baseline Covariate (Age) on CD4 count

	β_0 (SE)	
	Naive	Robust
Unweighted OLS	225.9 (9.9)	225.9 (12.6)
Weighted LS	225.9 (13.3)	225.9 (12.6)
	β_1 (SE)	
	Naive	Robust
Unweighted OLS	24.24 (14.2)	24.24 (19.3)
Weighted LS	24.24 (19.2)	24.24 (19.3)

Random Effects Model of CD4 vs. Baseline Age

– Fit simple random effects model: with same assumptions as above

$$Y_{ij} = \beta_0 + \beta_{0i} + \beta_1 X_{ij} + e_{ij}$$

```
. xtreg cd4 binage, i(id) re

Random-effects GLS regression                   Number of obs      =       594
Group variable (i): id                          Number of groups   =       297

R-sq:  within  =      .                         Obs per group: min =         2
       between = 0.0054                                        avg =       2.0
       overall = 0.0049                                        max =         2

Random effects u_i ~ Gaussian                   Wald chi2(1)       =      1.59
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.2075

------------------------------------------------------------------------------
         cd4 |      Coef.   Std. Err.       z     P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
est of β1 binage     24.2404   19.22938     1.26   0.207    -13.44848    61.92928
est of β0 _cons     225.902   13.38962    16.87   0.000     199.6588    252.1451
-------------+----------------------------------------------------------------
     sigma_u |  157.74218 estimate of  σ²0
     sigma_e |  71.379705 estimate of  σ²
         rho |  .83003801   (fraction of variance due to u_i)
------------------------------------------------------------------------------
```

Association of Time-Varying Covariate (Viral Load) on CD4 count.

- Binary VL: X_{ij} = 0 (<2000) or 1 (>2000) – all subjects included have one low and one high VL.
- Fit simple linear model:

$$E[Y_{ij} \mid X_{ij} = x_i] = \beta_0 + \beta_1 x_{ij}$$

- Compare results of Models A-D

	Naive	Robust
Unweighted OLS	A	B
Weighted LS	C	D

Summary of Results of Association of Time Varying Covariate (VL) on CD4 count (note, different data that last lecture)

β_0(SE)

	Naive	Robust
Unweighted OLS	355.1(21.7)	355.1(23.6))
Weighted LS	355.1(21.7)	355.1(22.9)

β_1(SE)

	Naive	Robust
Unweighted OLS	-79.3(30.7)	-79.3(17.1)
Weighted LS	-79.3(17.0)	-79.3(17.1)
t-test (difference)	-79.3(17.1)	

Random Effects Model of CD4 vs. $\log_{10}$(viral load)

– Fit simple random effects model: with same assumptions as above

$$Y_{ij} = \beta_0 + \beta_{0i} + \beta_1 X_{ij} + e_{ij}$$

```
. xtreg cd4 medvl, i(id) re

Random-effects GLS regression                   Number of obs      =       174
Group variable (i): id                          Number of groups   =        87

R-sq:  within  = 0.0000                         Obs per group: min =         2
       between = 0.0000                                        avg =       2.0
       overall = 0.0370                                        max =         2

Random effects u_i ~ Gaussian                   Wald chi2(1)       =     21.44
corr(u_i, X)       = 0 (assumed)                Prob > chi2        =    0.0000

------------------------------------------------------------------------------
         cd4 |      Coef.   Std. Err.       z     P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       medvl |  -79.34483   17.13523    -4.63   0.000    -112.9293   -45.76039
       _cons |   355.0805   21.80987    16.28   0.000     312.3339     397.827
-------------+----------------------------------------------------------------
     sigma_u |    169.148 estimate of  σ²0
     sigma_e |   113.0146 estimate of  σ²
         rho |  .69136617   (fraction of variance due to u_i)
------------------------------------------------------------------------------
```

Multiple and varying observations per person CD4 (Y) vs. continuous (log) Viral Load (X)

$$E[Y_{ij} \mid X_{i1} = x_{i1}, X_{ij} = x_{ij}] = \beta_0 + \beta_1 x_{i1} + \beta_2 (x_{ij} - x_{i1})$$

- β_2 represents the expected change in Y given a change in X_{ij} relative to the baseline value (X_{i1}) - <u>longitudinal effect</u>.

- β_1 represents the expected difference in average Y across two sub-populations that differ by their baseline values, X_{i1} - <u>cross-sectional effect.</u>

Summary of Results of Association of Time-Varying Covariate (VL) on CD4 count – multiple observations per person

	β_0(SE)	
	Naive	**Robust**
Unweighted OLS	618.9(11.6)	618.9(35.2)
Weighted LS	509.1(31.2)	509.1(32.9)
	β_1(SE)	
	Naive	**Robust**
Unweighted OLS	-83.7(3.0)	-83.7(8.3)
Weighted LS	-52.7(7.4)	-52.7(7.7)
	β_2(SE)	
	Naive	**Robust**
Unweighted OLS	-99.2(2.4)	-99.2(6.8)
Weighted LS	-54.7(2.2)	-54.7(3.2)

General Method for Choosing Random Effects/Correlation Model

- Choose fixed effects model – more elaborate the better.

- For every combination of random effects and correlation you would consider, fit the model using the same fixed effects model, record Aikake Information Criterion (AIC) – which is a fit statistic penalized by the number of parameters.

- Choose the model with the smallest AIC.

$AIC = -2*loglik+2*p$, p is the number of parameters

$$Y_{ij} = \beta_0 + \beta_{0i} + \beta_1 X_{i1} + \beta_2 (X_{ij} - X_{i1}) + e_{ij}$$

$$\sigma^2_{\beta_{0i}} \equiv \mathrm{var}(\beta_{0i}),\ \sigma^2_e \equiv \mathrm{var}(e_{ij})$$

```
. mixed cd4 logvlbase logvlchange || id:,  stddev
```

```
                                                Wald chi2(2)       =    832.00
Log likelihood = -43826.581                     Prob > chi2        =    0.0000

------------------------------------------------------------------------------
         cd4 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   logvlbase |  -52.05566   8.121493    -6.41   0.000    -67.97349   -36.13782
 logvlchange |  -53.47144   1.855169   -28.82   0.000    -57.10751   -49.83538
       _cons |   506.5567   34.39893    14.73   0.000     439.1361    573.9774
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
                  sd(_cons)  |    186.629   6.760737      173.8376    200.3615
-----------------------------+------------------------------------------------
               sd(Residual)  |   108.3884   .9402027      106.5612    110.2469
------------------------------------------------------------------------------
LR test vs. linear regression: chibar2(01) =  7437.72 Prob >= chibar2 = 0.0000
```

Row labels beside the output: $\hat{\beta}_1$ (logvlbase), $\hat{\beta}_2$ (logvlchange), $\hat{\beta}_0$ (_cons), $\hat{\sigma}_{\beta_{0i}}$ (sd(_cons)), $\hat{\sigma}_e$ (sd(Residual)).

Intraclass Correlation Coefficient and Measure of Fit (AIC)

```
. estat icc

Residual intraclass correlation

------------------------------------------------------------------------------
                       Level |        ICC   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
                          id |   .7477793   .0140775       .719203    .7743597
------------------------------------------------------------------------------
```

$$\frac{\hat{\sigma}^2_{\beta_{0i}}}{\hat{\sigma}^2_{\beta_{0i}} + \hat{\sigma}^2_e} = \frac{\text{Estimated Between Subject Variance}}{\text{Total Variance} = \text{var}(Y_{ij})}$$

```
. estat ic

Akaike's information criterion and Bayesian information criterion

-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
           . |   7053          .    -43826.58      5     87663.16    87697.47
-----------------------------------------------------------------------------
               Note:  N=Obs used in calculating BIC; see [R] BIC note
```

Re-do with *Robust* Standard Errors

```
. mixed cd4 logvlbase logvlchange || id:,  stddev cluster(id)

                                   (Std. Err. adjusted for 406 clusters in id)
------------------------------------------------------------------------------
             |               Robust
         cd4 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   logvlbase |  -52.05566     7.76666    -6.70   0.000    -67.27803   -36.83328
 logvlchange |  -53.47144    3.163293   -16.90   0.000    -59.67138    -47.2715
       _cons |   506.5567    33.09145    15.31   0.000     441.6987    571.4148
------------------------------------------------------------------------------

------------------------------------------------------------------------------
                             |               Robust
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
                   sd(_cons) |    186.629    9.162828      169.5072    205.4802
-----------------------------+------------------------------------------------
                sd(Residual) |   108.3884    3.435494      101.8598    115.3354
------------------------------------------------------------------------------
```

Random Coefficient Model

$$Y_{ij} = (\beta_0 + \beta_{0i}) + \beta_1 X_{i1} + (\beta_2 + \beta_{2i}) * (X_{ij} - X_{i1}) + e_{ij}$$

$$\sigma^2_{\beta_{0i}} \equiv \mathrm{var}(\beta_{0i}),\ \sigma^2_{\beta_{2i}} \equiv \mathrm{var}(\beta_{2i}), \sigma^2_e \equiv \mathrm{var}(e_{ij}), \sigma_{10} \equiv \mathrm{cov}(\beta_{0i}, \beta_{2i})$$

```
. mixed cd4 logvlbase logvlchange || id: logvlchange,
    stddev  cov(unstruct)
```

	cd4	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
$\hat{\beta}_1$	logvlbase	-66.69168	6.935967	-9.62	0.000	-80.28593	-53.09743
$\hat{\beta}_2$	logvlchange	-54.16069	2.975448	-18.20	0.000	-59.99246	-48.32892
$\hat{\beta}_0$	_cons	553.9275	28.89506	19.17	0.000	497.2942	610.5607

	Random-effects Parameters	Estimate	Std. Err.	[95% Conf.	Interval]
	id: Unstructured				
$\hat{\sigma}_{\beta 2i}$	sd(logvlc~e)	41.14181	2.911627	35.81322	47.26323
$\hat{\sigma}_{\beta_{0i}}$	sd(_cons)	164.0304	6.245377	152.2353	176.7394
$\hat{cor}(\beta_{0i}, \beta_{2i})$	corr(logvlc~e,_cons)	-.5886842	.0676882	-.7057546	-.4403184
$\hat{\sigma}_e$	sd(Residual)	104.7828	.9310012	102.9739	106.6235

```
LR test vs. linear regression:      chi2(3) =  7729.27   Prob > chi2 = 0.0000
.
```

Fit Statistics

```
. estat ic

Akaike's information criterion and Bayesian information criterion

-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
           . |   7053           .    -43680.8      7     87375.61    87423.63
-----------------------------------------------------------------------------
```

Re-do with Robust Estimated of Variance

```
. mixed cd4 logvlbase logvlchange || id: logvlchange,  stddev  cov(unstruct) cluster(id)

                                  (Std. Err. adjusted for 406 clusters in id)
------------------------------------------------------------------------------
             |               Robust
         cd4 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   logvlbase |  -66.69168   7.022014    -9.50   0.000    -80.45458   -52.92879
 logvlchange |  -54.16069   3.008829   -18.00   0.000    -60.05789   -48.26349
       _cons |   553.9275   30.89291    17.93   0.000     493.3785    614.4765
------------------------------------------------------------------------------

------------------------------------------------------------------------------
                             |               Robust
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Unstructured             |
                sd(logvlc~e) |   41.14181   3.762318      34.39086    49.21797
                   sd(_cons) |   164.0304   8.518709      148.1557    181.6061
         corr(logvlc~e,_cons) |  -.5886842   .0836119     -.7289279   -.4010203
-----------------------------+------------------------------------------------
                sd(Residual) |   104.7828   3.357696      98.40426    111.5748
------------------------------------------------------------------------------
```

Model	Parameter	Estimate	SE(Naïve)	SE(Robust)
Simple Random Effects $Y_{ij} = \beta_0 + \beta_{0i} + \beta_1 X_{i1} + \beta_2 (X_{ij} - X_{i1}) + e_{ij}$	β_0	506.5	34.4	33.1
	β_1	-52.1	8.1	7.8
	β_2	-53.5	1.8	3.2
	$SD(\beta_{0i})$	186.6	6.8	9.2
	$SD(e_{ij})$	108.4	0.94	3.4
	ICC	0.75	0.014	N/A
Fit Statistic	AIC	87663		
Random Coefficients $Y_{ij} = (\beta_0 + \beta_{0i}) + \beta_1 X_{i1} + (\beta_2 + \beta_{2i})(X_{ij} - X_{i1}) + e_{ij}$	β_0	553.9	28.9	30.9
	β_1	-66.7	6.9	7.0
	β_2	-54.2	3.0	3.0
	$SD(\beta_{0i})$	164.0	6.2	8.5
	$SD(\beta_{2i})$	41.1	2.9	3.8
	$SD(e_{ij})$	104.8	0.93	3.4
	$Cor(\beta_{0i}, \beta_{2i})$	-0.59	0.068	0.084
Fit Statistic	AIC	87375	Smaller than above	***

Using Estimated Random Coefficients Distributions

$$Y_{ij} = (\beta_0 + \beta_{0i}) + \beta_1 X_{i1} + (\beta_2 + \beta_{2i})(X_{ij} - X_{i1}) + e_{ij}$$

- This estimated distribution of β_{2i} can be used to estimate the quartiles of the longitudinal effect of changes in log10 viral load across the population.

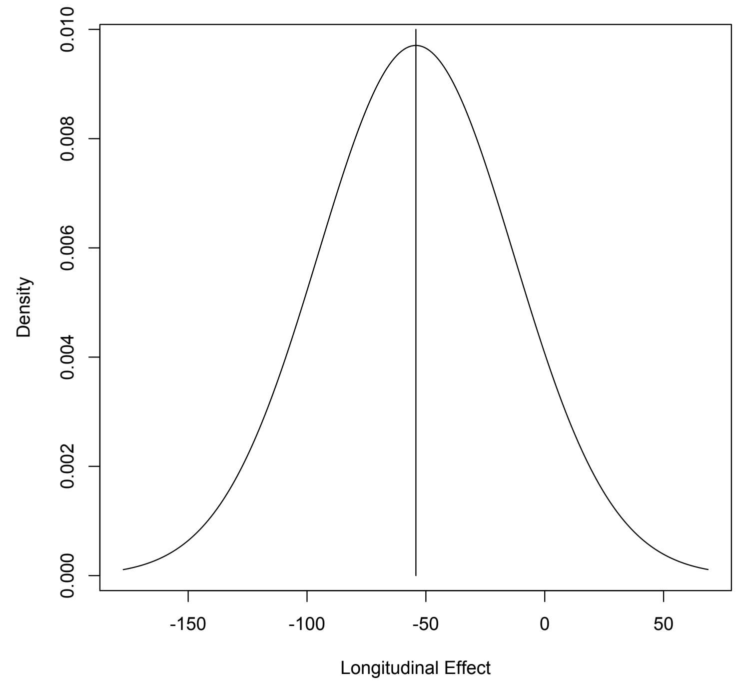
- Specifically, the estimated distribution of the longitudinal effect is ~ Normal with mean -54.2 and standard deviation 41.1.

Using Estimated Longitudinal Effect Distribution to exam how it might vary in population

Estimated IQR then is

$$(\hat{\beta}_2 - Z_{0.75} * \hat{\sigma}_{\beta_{2i}}, \hat{\beta}_2 + Z_{0.75} * \hat{\sigma}_{\beta_{2i}})$$

or,




```
. display "("-54.2-invnormal(0.75)*41.1 " , „ -54.2+invnormal(0.75)*41.1 " )"
```

```
(-81.921529 , -26.478471 )
```

Strength Data

- Subjects randomized to one of 3 treatments

1. No training (tx=1)
2. Weight training with light weights and high repetition (tx=2)
3. Weight training with heavy weights and low repetition (tx=3)

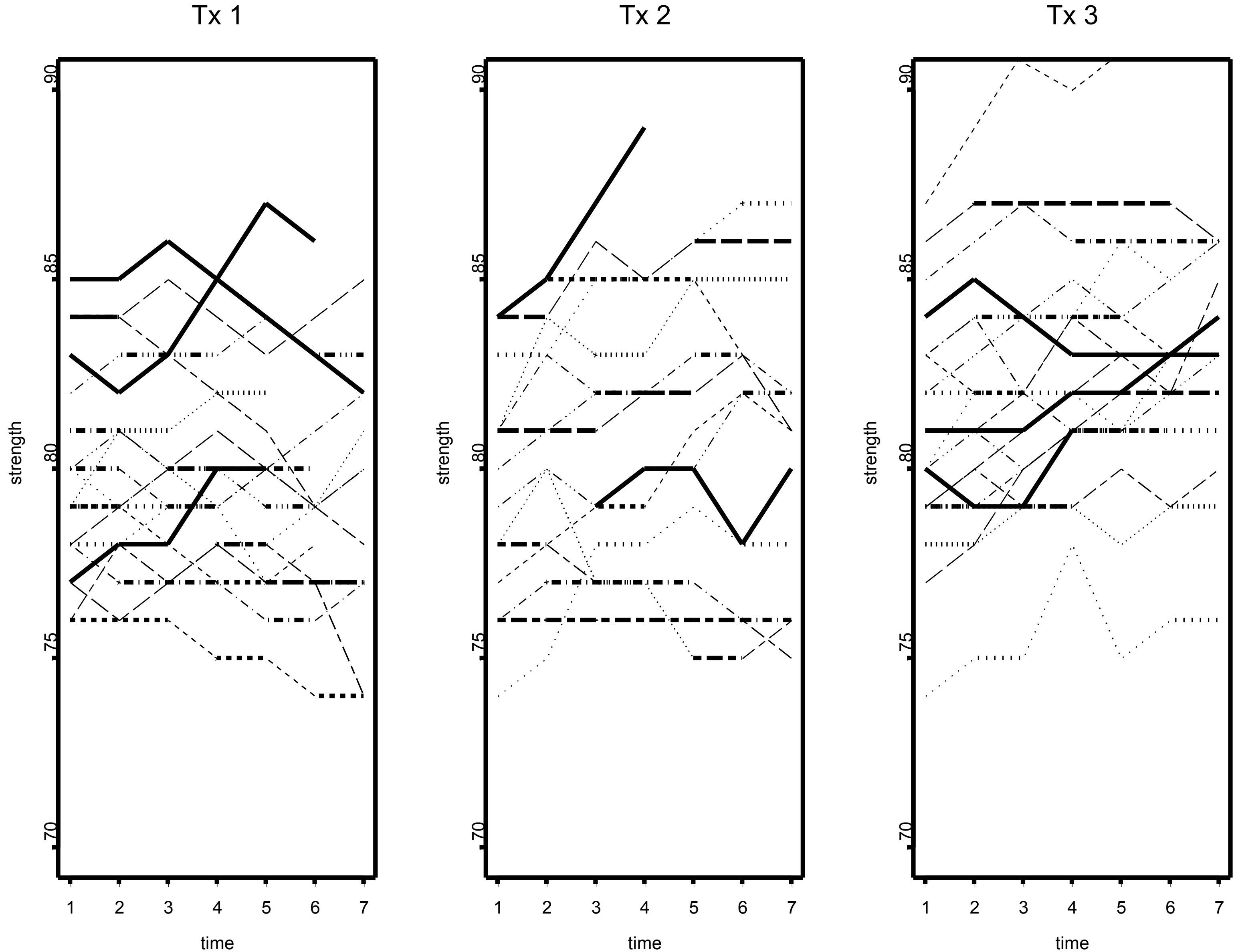
- Subjects were followed for 7 weeks and a measure of muscle strength was recorded each week.

- The questions of interest are

1. Does weight training have any impact on strength?
2. Is there a difference between tx 2 and 3?
3. Which training program works quickest to increase strength?

Strength Data

	id	tx	y	time
1.	1	1	85	1
2.	1	1	85	2
3.	1	1	86	3
4.	1	1	85	4
5.	1	1	87	5
6.	1	1	86	6
7.	1	1	.	7
8.	2	1	80	1
9.	2	1	79	2
10.	2	1	.	3
11.	2	1	78	4
12.	2	1	78	5
13.	2	1	79	6
14.	2	1	.	7


Tx 1
Tx 2
Tx 3
strength
time
90
85
80
75
70
1
2
3
4
5
6
7

Mixed Model I for Strength Data

- First, the Model (X_{ij}, time of ijth measurement, Tx_i is the treatment assignment for ith person).

$$Y_{ij} = \left(\beta_0 + \beta_{0i}\right) + \beta_1 X_{ij} +$$
$$\beta_2 I(Tx_i = 1) + \beta_3 I(Tx_i = 2) +$$
$$\beta_4 I(Tx_i = 1) * X_{ij} + \beta_5 I(Tx_i = 2) * X_{ij} + e_{ij}$$

- $E(\beta_{0i})=0$, $E(e_{ij})=0$.
- Var(β_{0i})= σ^2_0, Var(e_{ij})= σ^2
- cov(β_{0i}, e_{ij})=0.
- What are the fixed and random effects in this model?

STATA for Strength Data - XTREG

```
. gen tx1 = tx==1
. gen tx2 = tx==2
. gen tx1time = tx1*time
. gen tx2time = tx2*time

. xtmixed y tx1 tx2 time tx1time tx2time || id:,  stddev

Computing standard errors:

Mixed-effects ML regression                     Number of obs      =       370
Group variable: id                              Number of groups   =        57

                                                Obs per group: min =         5
                                                               avg =       6.5
                                                               max =         7


                                                Wald chi2(5)       =     69.34
Log likelihood = -663.52557                     Prob > chi2        =    0.0000

------------------------------------------------------------------------------
           y |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         tx1 |  -.9568027   .9747114    -0.98   0.326    -2.867202    .9535965
         tx2 |  -1.148717   1.035119    -1.11   0.267    -3.177514    .8800792
        time |   .3038536   .0482746     6.29   0.000     .2092371    .3984701
     tx1time |  -.3731916   .0680399    -5.48   0.000    -.5065475   -.2398358
     tx2time |  -.0611408   .0714343    -0.86   0.392    -.2011495    .0788679
       _cons |    81.0185   .6810689   118.96   0.000     79.68363    82.35337
------------------------------------------------------------------------------
```

Variance Components

```
------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
                   sd(_cons) |   2.977532    .284653      2.468774    3.591134
-----------------------------+------------------------------------------------
                sd(Residual) |   1.074968    .042967      .9939687    1.162569
------------------------------------------------------------------------------
LR test vs. linear regression: chibar2(01) =   571.45 Prob >= chibar2 = 0.0000

. estat icc

Residual intraclass correlation

------------------------------------------------------------------------------
                       Level |        ICC   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
                          id |   .8846894   .0212074      .8361909    .9201994
------------------------------------------------------------------------------
. estat ic

Akaike's information criterion and Bayesian information criterion

-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
           . |    370           .   -663.5256      8     1343.051    1374.359
-----------------------------------------------------------------------------
```

STATA for Strength Data, cont.

- Test of no treatment effect, H_0: $\beta_4 = \beta_5 = 0$

```
. test tx1time tx2time

 ( 1)   [y]tx1time = 0
 ( 2)   [y]tx2time = 0

           chi2(  2) =   34.17
         Prob > chi2 =    0.0000
```

Re-do with robust SE's

```
. xtmixed y tx1 tx2 time tx1time tx2time || id:,  stddev  cluster(id)

                                                Wald chi2(5)       =     33.81
Log pseudolikelihood = -663.52557               Prob > chi2        =    0.0000

                                     (Std. Err. adjusted for 57 clusters in id)
------------------------------------------------------------------------------
             |               Robust
           y |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         tx1 |  -.9568027   .9449005    -1.01   0.311    -2.808774    .8951683
         tx2 |  -1.148717   1.056909    -1.09   0.277     -3.22022    .9227856
        time |   .3038536   .0699036     4.35   0.000     .1668452    .4408621
     tx1time |  -.3731916    .103697    -3.60   0.000     -.576434   -.1699493
     tx2time |  -.0611408   .1321063    -0.46   0.643    -.3200644    .1977829
       _cons |    81.0185   .7301918   110.96   0.000     79.58735    82.44965
------------------------------------------------------------------------------
```

Re-do with robust SE's

```
------------------------------------------------------------------------------
                             |               Robust
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
                   sd(_cons) |   2.977532   .2615252      2.506646    3.536876
-----------------------------+------------------------------------------------
                sd(Residual) |   1.074968   .0642565      .9561254    1.208583
------------------------------------------------------------------------------

. test tx1time tx2time

 ( 1)  [y]tx1time = 0
 ( 2)  [y]tx2time = 0

           chi2(  2) =   13.72
         Prob > chi2 =    0.0010
```

Equivalent STATA for Strength Data, XTGEE with exchangeable

```
.xtgee y tx1 tx2 time tx1time tx2time, i(id) cor(exc)


GEE population-averaged model                   Number of obs      =       370
Group variable:                         id      Number of groups   =        57
Link:                             identity      Obs per group: min =         5
Family:                           Gaussian                     avg =       6.5
Correlation:                  exchangeable                     max =         7
                                                Wald chi2(5)       =     64.83
Scale parameter:                  9.918406      Prob > chi2        =    0.0000

------------------------------------------------------------------------------
           y |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         tx1 |   -.956994   .9684046    -0.99   0.323    -2.855032    .9410442
         tx2 |  -1.148591   1.028411    -1.12   0.264    -3.164239    .8670575
        time |   .3037201   .0501318     6.06   0.000     .2054634    .4019767
     tx1time |  -.3730803   .0706584    -5.28   0.000    -.5115681   -.2345924
     tx2time |  -.0611578   .0741834    -0.82   0.410    -.2065545    .0842389
       _cons |    81.0188   .6766896   119.73   0.000     79.69251    82.34509
------------------------------------------------------------------------------

.
```

Equivalent STATA for Strength Data, XTGEE with exchangeable

```
. xtcorr
```

	c1	c2	c3	c4	c5	c6	c7
r1	1.0000						
r2	0.8743	1.0000					
r3	0.8743	0.8743	1.0000				
r4	0.8743	0.8743	0.8743	1.0000			
r5	0.8743	0.8743	0.8743	0.8743	1.0000		
r6	0.8743	0.8743	0.8743	0.8743	0.8743	1.0000	
r7	0.8743	0.8743	0.8743	0.8743	0.8743	0.8743	1.0000

Equivalent STATA for Strength Data, XTGEE with exchangeable, robust

```
. xtgee y tx1 tx2 time tx1time tx2time, i(id) cor(exc) robust

GEE population-averaged model                   Number of obs      =       370
Group variable:                         id      Number of groups   =        57
Link:                             identity      Obs per group: min =         5
Family:                           Gaussian                     avg =       6.5
Correlation:                  exchangeable                     max =         7
                                                Wald chi2(5)       =     33.82
Scale parameter:                  9.918406      Prob > chi2        =    0.0000

                                    (standard errors adjusted for clustering on id)
------------------------------------------------------------------------------
             |             Semi-robust
           y |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         tx1 |   -.956994   .9449735    -1.01   0.311    -2.809108      .89512
         tx2 |  -1.148591   1.057032    -1.09   0.277    -3.220334    .9231534
        time |   .3037201   .0698707     4.35   0.000     .1667761     .440664
     tx1time |  -.3730803   .1036701    -3.60   0.000      -.57627   -.1698906
     tx2time |  -.0611578   .1320877    -0.46   0.643    -.3200449    .1977294
       _cons |    81.0188   .7302755   110.94   0.000     79.58749    82.45011
------------------------------------------------------------------------------
```

Mixed Model II for Strength Data (Random Coefficients Model)

- The Model:

$$Y_{ij} = \left(\beta_0 + \beta_{0i}\right) + (\beta_1 + \beta_{1i})X_{ij} +$$
$$\beta_2 I(Tx_i = 1) + \beta_3 I(Tx_i = 2) +$$
$$\beta_4 I(Tx_i = 1) * X_{ij} + \beta_5 I(Tx_i = 2) * X_{ij} + e_{ij}$$

- $E(\beta_{0i})=0$, $E(\beta_{1i})=0$, $E(e_{ij})=0$.

- $\mathrm{Var}(\beta_{0i}) = \sigma^2{}_0$, $\mathrm{Var}(\beta_{1i}) = \sigma^2{}_1$, $\mathrm{Var}(e_{ij}) = \sigma^2$

- $\mathrm{cov}(\beta_{0i}, \beta_{1i}) = \sigma_{12}$, $\mathrm{cov}(\beta_{0i}, e_{ij})=0$, $\mathrm{cov}(\beta_{1i}, e_{ij})=0$.

Model II

```
. xtmixed y tx1 tx2 time tx1time tx2time || id: time,  stddev  cov(un)

Mixed-effects ML regression                     Number of obs      =       370
Group variable: id                              Number of groups   =        57

                                                Obs per group: min =         5
                                                               avg =       6.5
                                                               max =         7


                                                Wald chi2(5)       =     26.99
Log likelihood = -621.59666                     Prob > chi2        =    0.0001

------------------------------------------------------------------------------
           y |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         tx1 |  -.8791863   .9353663    -0.94   0.347    -2.712471     .954098
         tx2 |  -1.033765   .9932793    -1.04   0.298    -2.980556    .9130267
        time |   .3360225   .0821817     4.09   0.000     .1749494    .4970957
     tx1time |  -.4004078   .1169682    -3.42   0.001    -.6296614   -.1711543
     tx2time |   -.101627    .123829    -0.82   0.412    -.3443273    .1410734
       _cons |   80.93097   .6536334   123.82   0.000     79.64987    82.21207
------------------------------------------------------------------------------
```

Model II, cont

```
------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Unstructured             |
                   sd(time) |   .3337638   .0395831      .2645392    .4211031
                  sd(_cons) |   2.907665   .2887834      2.393342    3.532515
           corr(time,_cons) |  -.1421759   .1489017     -.4144803    .1534946
-----------------------------+------------------------------------------------
               sd(Residual) |   .8151804   .0360695      .7474643    .8890313
------------------------------------------------------------------------------
LR test vs. linear regression:       chi2(3) =   655.31   Prob > chi2 = 0.0000

. estat icc

Conditional intraclass correlation

------------------------------------------------------------------------------
                       Level |        ICC   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
                          id |   .9271284   .0148245      .8921923    .9513603
------------------------------------------------------------------------------
Note: ICC is conditional on zero values of random-effects covariates.

. estat ic
Akaike's information criterion and Bayesian information criterion

-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
           . |    370           .   -621.5967     10     1263.193    1302.328
-----------------------------------------------------------------------------
```

Model II, cont

```
. test tx1time tx2time

 ( 1)  [y]tx1time = 0
 ( 2)  [y]tx2time = 0

           chi2(  2) =   12.49
         Prob > chi2 =    0.0019
```

Model II, robust SE

```
. xtmixed y tx1 tx2 time tx1time tx2time || id: time,  stddev  cov(un)
    cluster(id)

                                  (Std. Err. adjusted for 57 clusters in id)
------------------------------------------------------------------------------
             |               Robust
           y |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         tx1 |  -.8791863   .9320558    -0.94   0.346    -2.705982    .9476095
         tx2 |  -1.033765   1.054272    -0.98   0.327      -3.1001     1.03257
        time |   .3360225   .0760073     4.42   0.000     .1870509    .4849942
     tx1time |  -.4004078   .1064014    -3.76   0.000    -.6089508   -.1918649
     tx2time |   -.101627   .1363948    -0.75   0.456    -.3689559     .165702
       _cons |   80.93097   .7207356   112.29   0.000     79.51836    82.34359
------------------------------------------------------------------------------

------------------------------------------------------------------------------
                             |               Robust
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Unstructured             |
                    sd(time) |   .3337638   .0417162      .2612461    .4264112
                   sd(_cons) |   2.907665   .2469605      2.461774    3.434319
             corr(time,_cons) |  -.1421759   .1668982     -.4438449    .1884383
-----------------------------+------------------------------------------------
                sd(Residual) |   .8151804    .044396       .732649    .9070089
------------------------------------------------------------------------------
```

Comparison of Results for Strength Data

Variable	Coef.	SE Simple Random Effects Model	SE GEE exch., not robust	SE GEE exch., robust	Coef. Random Coeff. Model	SE Random Coeff. Model
tx1	-0.96	0.975	0.968	0.945	-0.878	0.935
tx2	-1.15	1.035	1.028	1.057	-1.034	0.993
time	0.30	0.048	0.050	0.070	0.336	0.082
tx1time	-0.37	0.068	0.071	0.104	-0.400	0.117
tx2time	-0.06	0.071	0.074	0.132	-0.102	0.124
_cons	81.02	0.681	0.677	0.730	80.931	0.654
AIC	**1343**				**1263**	

General Method for Choosing Random Effects/Correlation Model

- Choose fixed effects model – more elaborate the better.

- For every combination of random effects and correlation you would consider, fit the model using the same fixed effects model, record Aikake Information Criterion (AIC) – which is a fit statistic penalized by the number of parameters.

- Choose the model with the smallest AIC.

*AIC = -2*loglik+2*p*, *p* is the number of parameters