Foley Retreat Research Methods Workshop: Introduction to Hierarchical Modeling

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FIELDS
Fostering Improvement in End-of-Life Decision Science

Learning objectives

1. List types of “hierarchically-organized” or “clustered” data.
2. Describe errors in inference that may arise if the structure of the data is not taken into account in the statistical analysis.
3. Differentiate between the main statistical approaches to hierarchical data.
4. Identify an example in your own research portfolio that may benefit from one of these approaches.

Outline

1. Explain hierarchical modeling conceptually
2. Explain hierarchical modeling mathematically
3. Review examples from the presenters’ research relevant to palliative and end-of-life care

Hierarchical or Multilevel Models

- The class is called “variance-component” models; also called:
  - Mixed models
  - Heirarchical models
  - Multi-level models

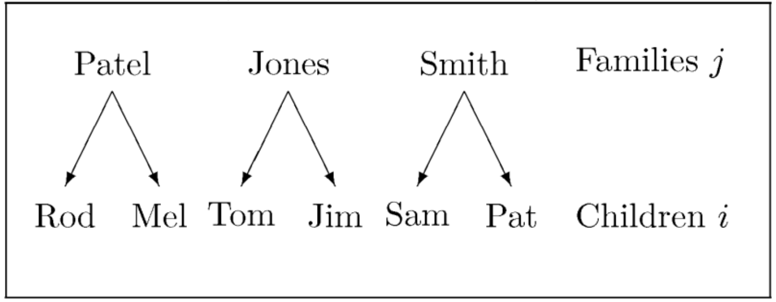
Conceptual explanation

Data

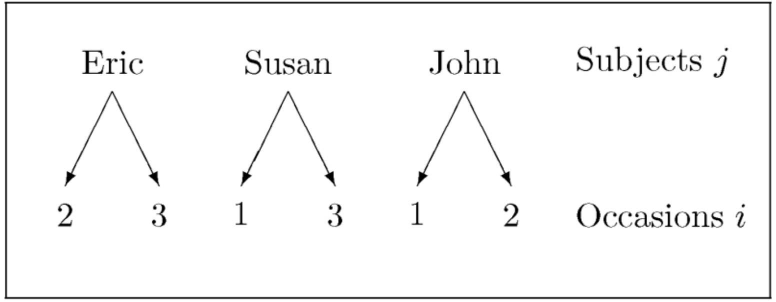
Why can't we use ordinary linear regression in these cases?

Rabe-Hesketh & Skrondal (2012): Multilevel and Longitudinal Modeling Using Stata

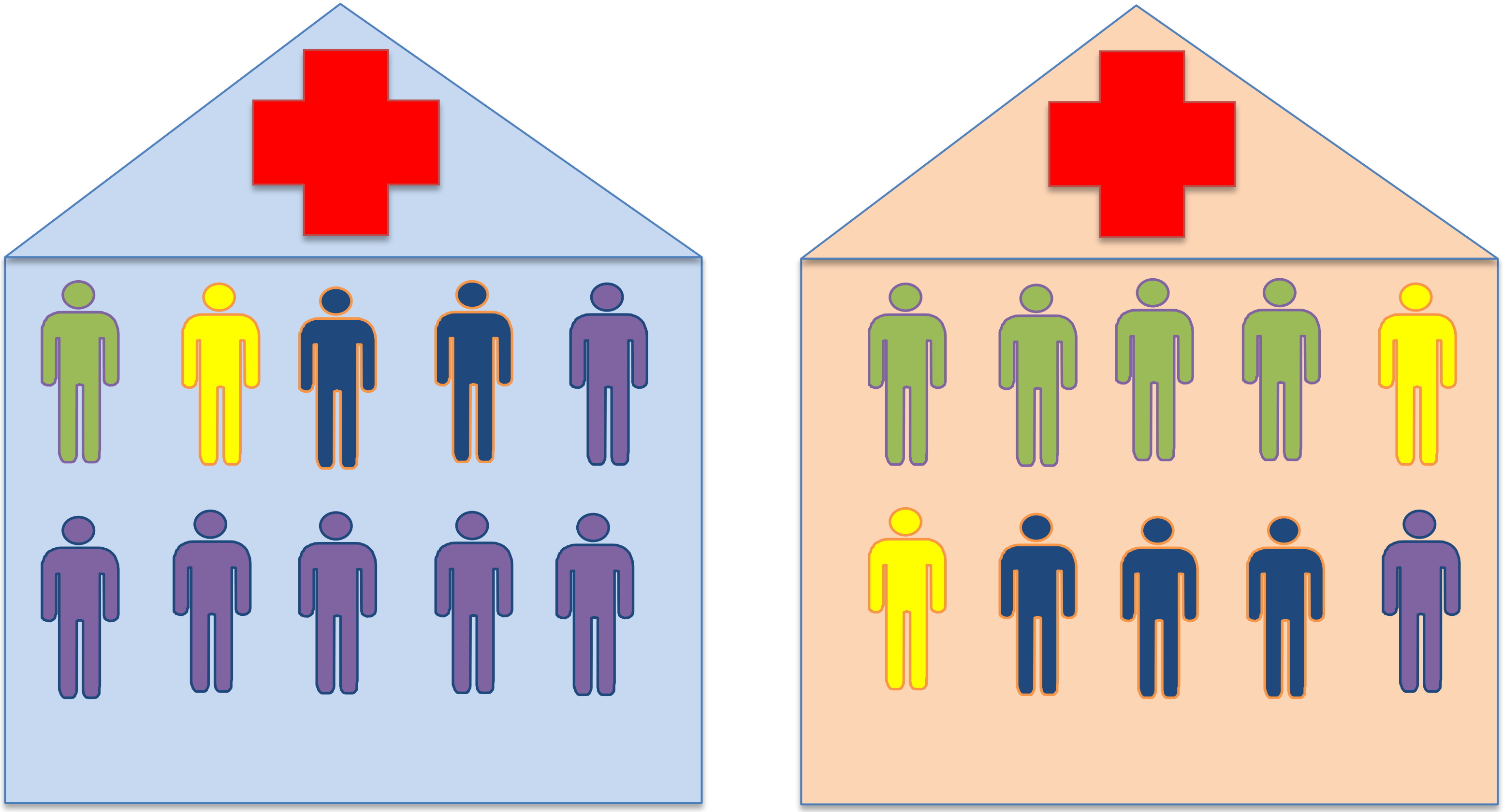
Children nested in families
(Cross-sectional data)



Occasions nested in subjects
(Longitudinal data)

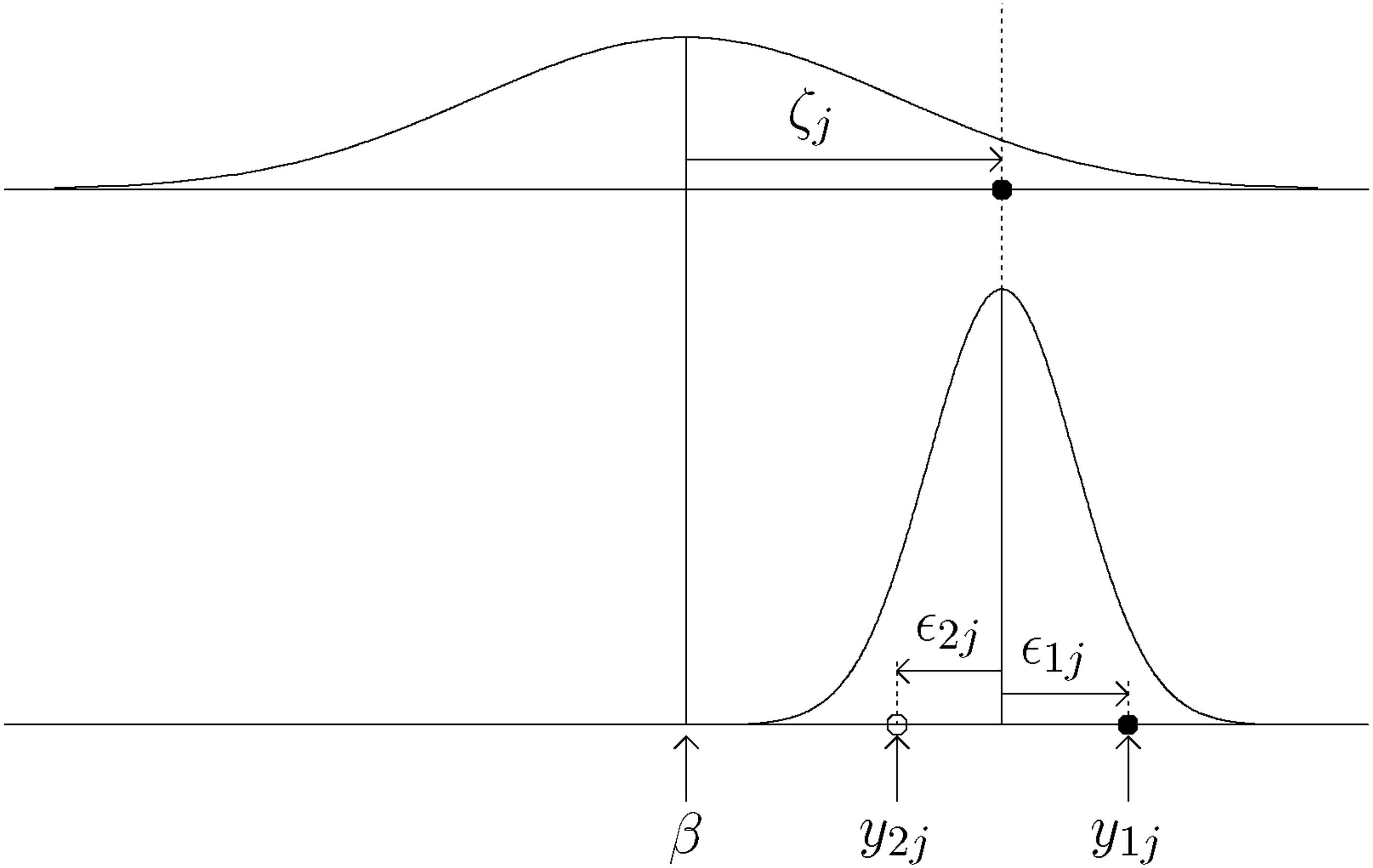


Non-independent observations



Statistical explanation

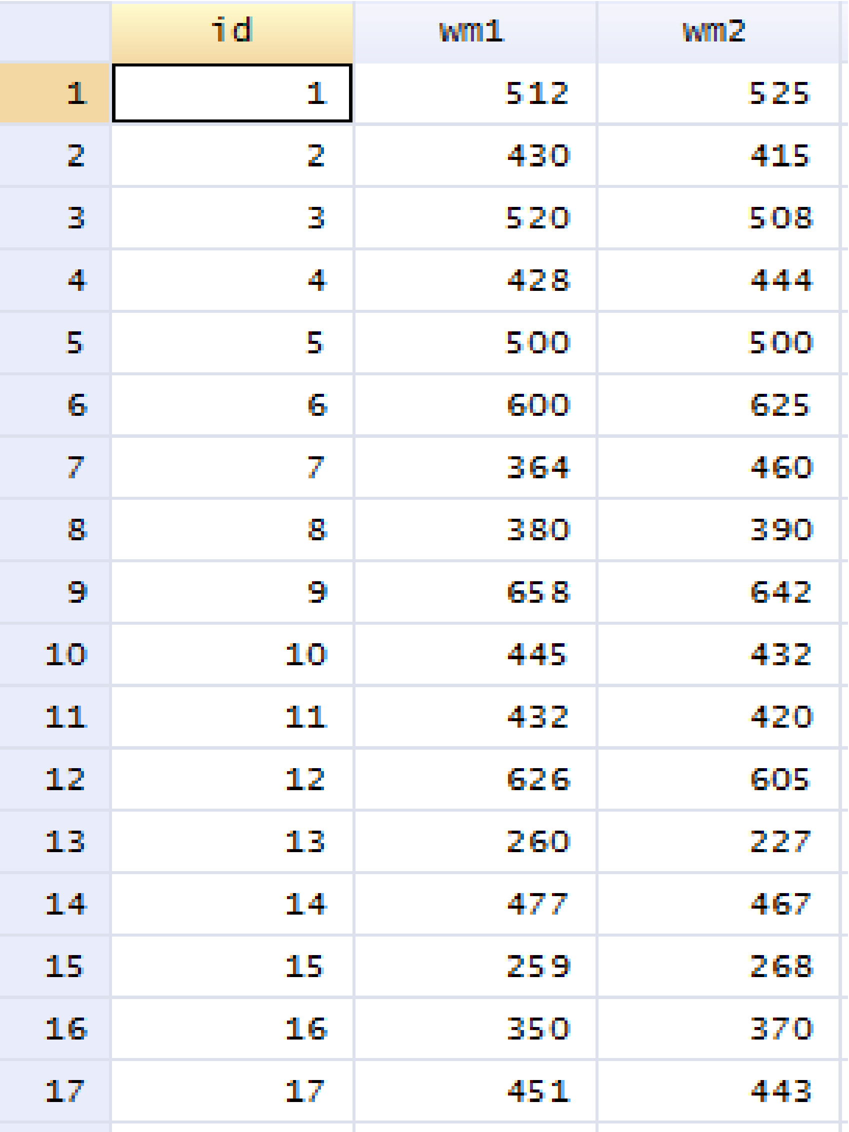
Rabe-Hesketh & Skrondal (2012): Multilevel and Longitudinal Modeling Using Stata



Repeated measures example (PEFR)

- Longitudinal data:
  - Level-1 unit: time/occasion/visit
  - Level-2 unit: subject

PEFR Dataset

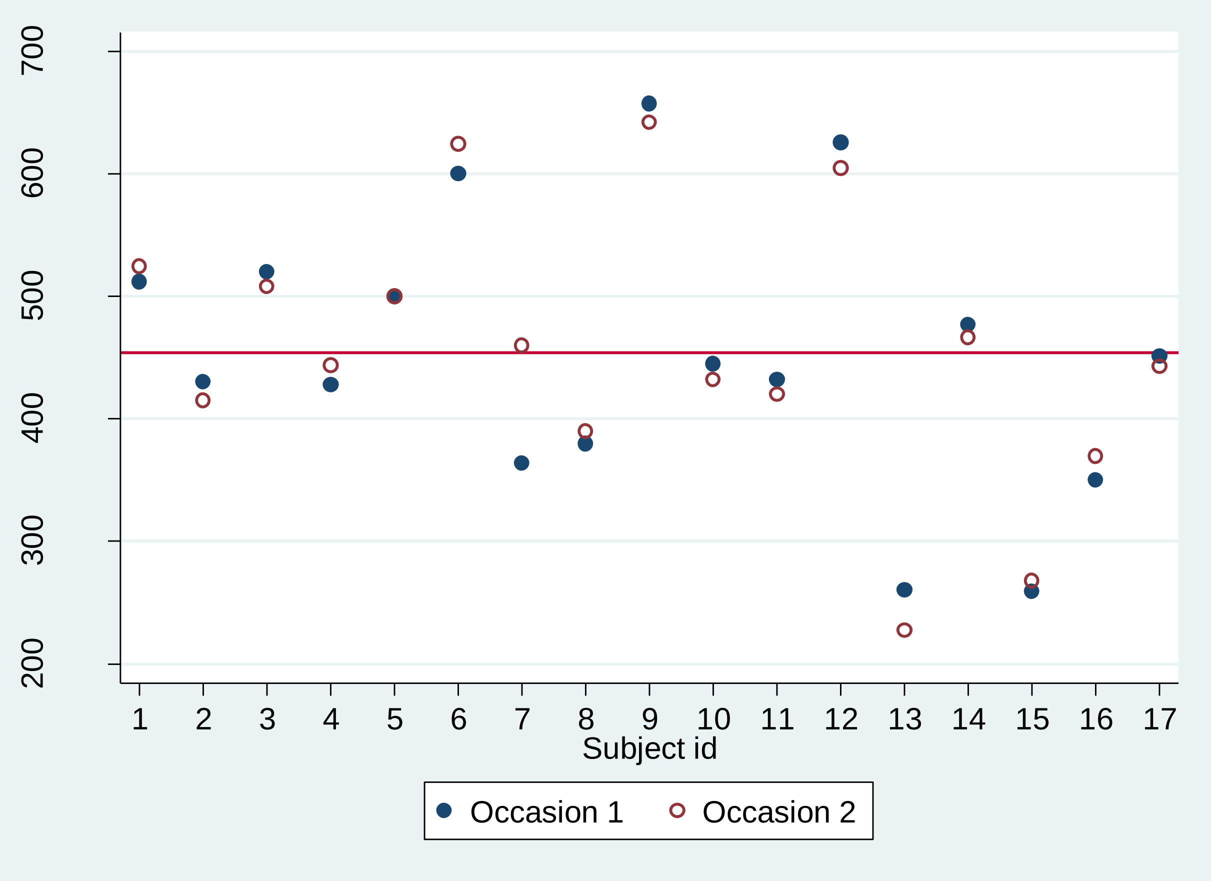


	id	wm1	wm2
1	1	512	525
2	2	430	415
3	3	520	508
4	4	428	444
5	5	500	500
6	6	600	625
7	7	364	460
8	8	380	390
9	9	658	642
10	10	445	432
11	11	432	420
12	12	626	605
13	13	260	227
14	14	477	467
15	15	259	268
16	16	350	370
17	17	451	443

- Peak-expiratory-flow rate (PERF) example
  - Reliability study to assess the quality of instruments to measure PEFR
  - N=17 had PEFR measured (L/min) twice
  - used the new Wright Mini (WM) peak-flow meter

PEFR Dataset…

- WM 1st and 2nd recordings by subject ID
  - Horizontal line: overall mean



- Within a subject, how far are the 2 measurements from each other?
- How far are the subject-specific means from the overall mean?

Random Intercept Model

Model:

$$y_{ij} = \beta + \zeta_j + \varepsilon_{ij}$$

Response/outcome of the i^{th} occasion for subject j

Overall mean

Random subject effect (Intercept) $\sim N(0,\psi)$

Random error $\sim N(0,\theta)$

2-level model:

- Level-1 unit: occasion
- Level-2 unit: subject

Sources of variations?

Random Intercept Model

Assumptions:

- Each error term (or variance component) is normally distributed with mean zero

$$\zeta_j \sim N(0,\psi)$$

$$\varepsilon_{ij} \sim N(0,\theta) \qquad \Rightarrow \mathrm{E}(y_{ij}) = \beta$$

- Variance components are uncorrelated

$$\mathbf{Cov}(\varepsilon_{ij},\zeta_j) = 0 \qquad \Rightarrow \mathbf{Var}(y_{ij}) = \psi + \theta$$

- Covariance of any 2 observations within the same subject:

$$\mathbf{Cov}(y_{ij}, y_{i'j}) = \psi \qquad , i \neq i'$$

- Observations from different subjects uncorrelated

$$\mathbf{Cov}(y_{ij}, y_{ij'}) = 0 \qquad , j \neq j'$$

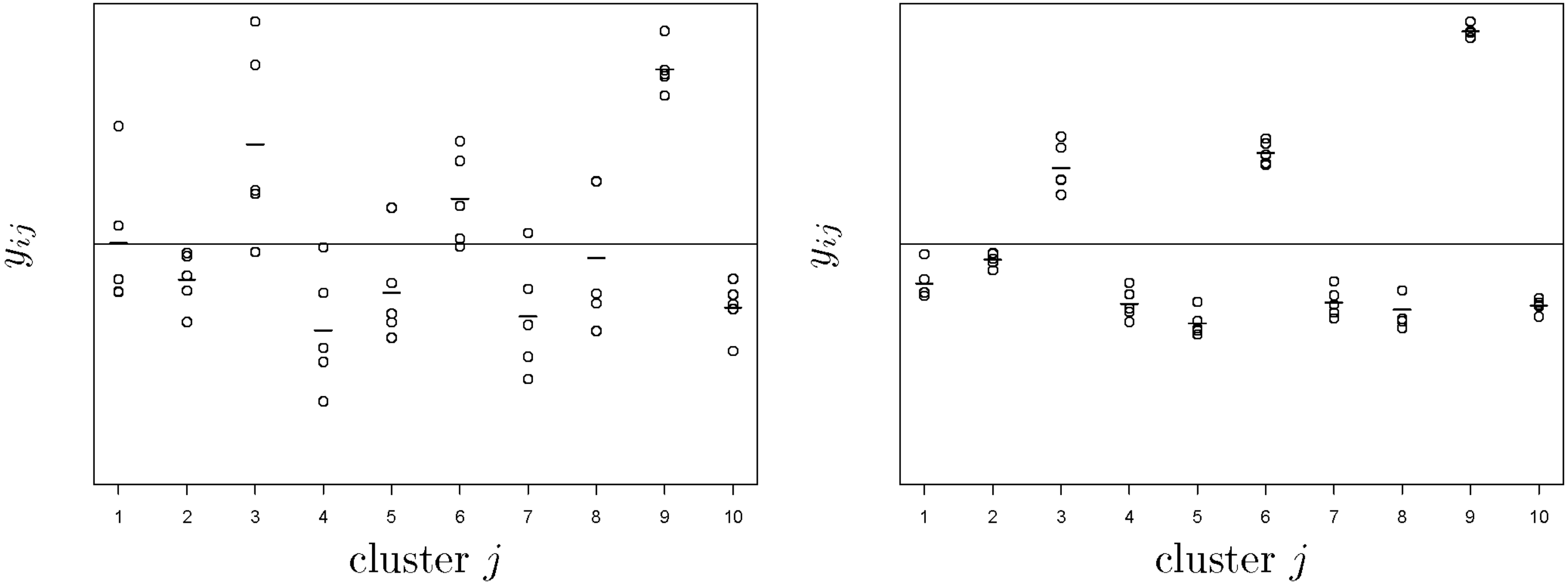
Intra-Class Correlation (ICC)

- Of interest is the proportion of the overall variability that can be attributed to subject-to-subject differences, or the intra-class correlation.

$$\rho = \frac{Var\left(\zeta_j\right)}{Var\left(y_{ij}\right)} = \frac{\psi}{\psi + \theta}$$

  - The more differences there are between subjects (relative to within), the higher the ICC.
  - like R^2 in ordinary regression

Rabe-Hesketh & Skrondal (2012): Multilevel and Longitudinal Modeling Using Stata



A

B

Which data has higher ICC? B

Estimation using Stata

- To obtain the MLE for variance-component models (such as the random intercept model), use `mle` option for either:
  - `xtreg`
  - `xtmixed`
- `xtreg` more efficient, but postestimation commands of `xtmixed` more useful
- Data needs to be in the long format

PEFR Example

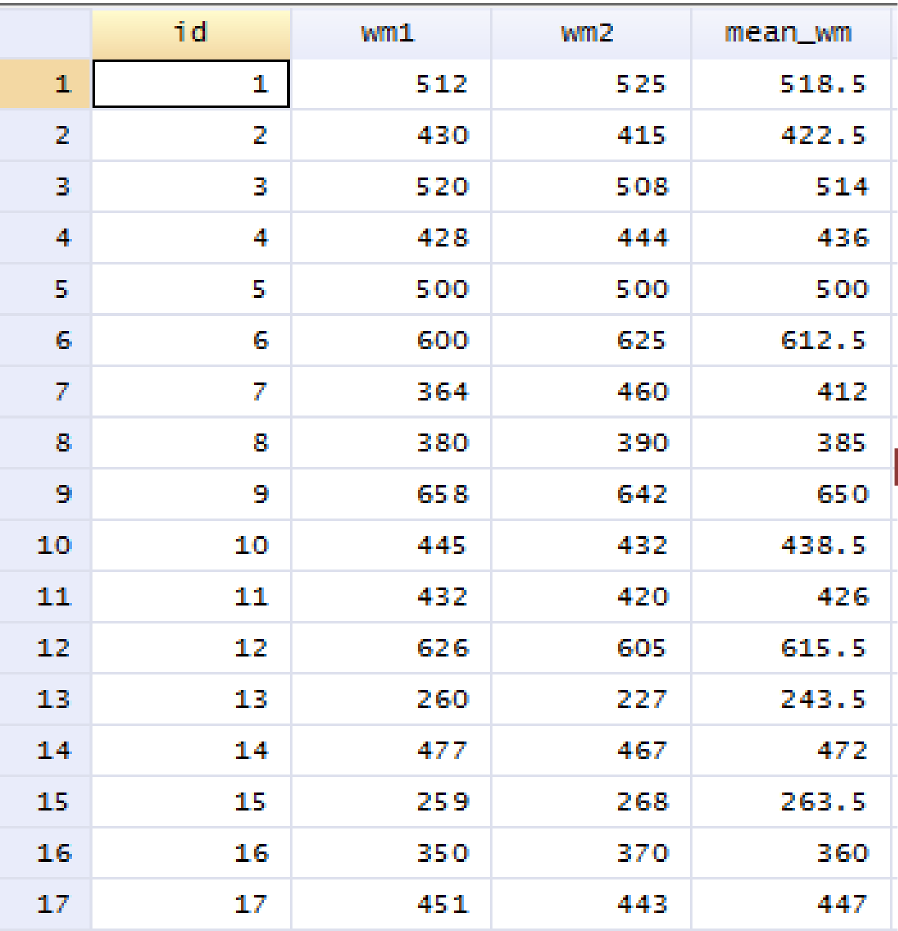
Reshape the data:

level-2

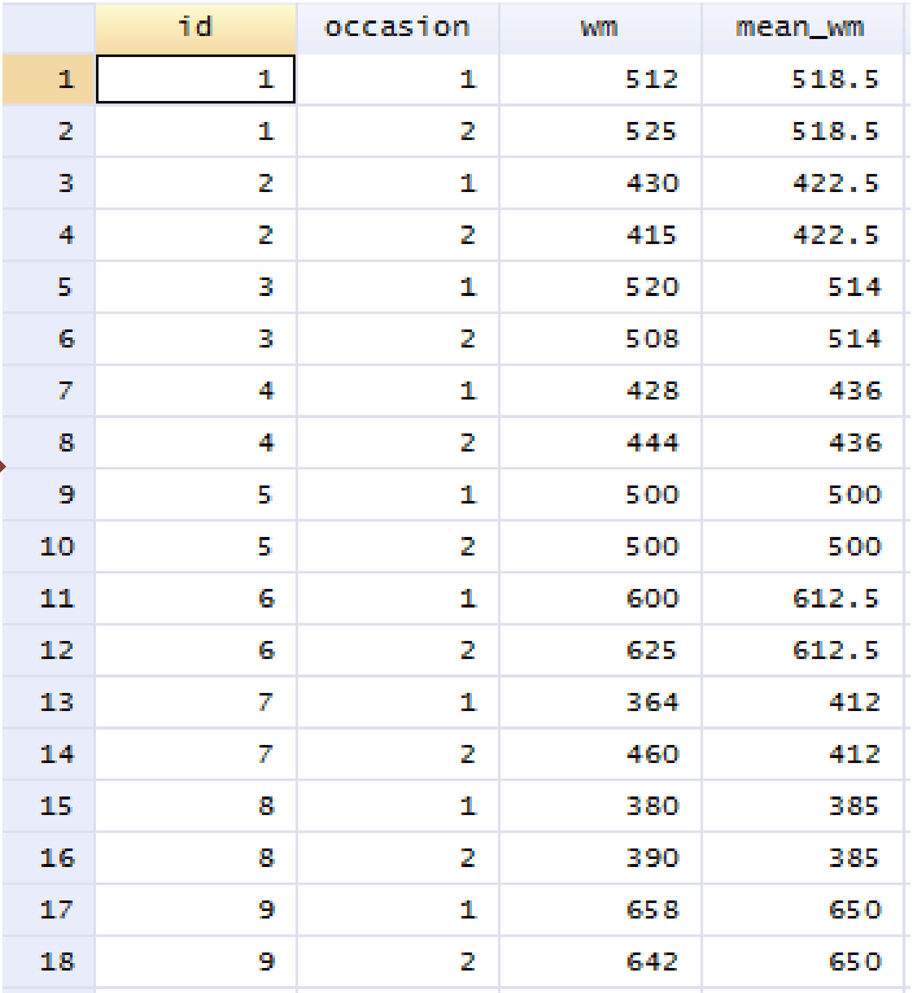
level-1

```
. reshape long wm, i(id) j(occasion)
(note: j = 1 2)

Data                               wide   ->   long
-----------------------------------------------------------------------------
Number of obs.                       17   ->      34
Number of variables                   4   ->       4
j variable (2 values)                     ->   occasion
xij variables:
                                wm1 wm2   ->   wm
-----------------------------------------------------------------------------
```

PEFR Example...



	id	wm1	wm2	mean_wm
1	1	512	525	518.5
2	2	430	415	422.5
3	3	520	508	514
4	4	428	444	436
5	5	500	500	500
6	6	600	625	612.5
7	7	364	460	412
8	8	380	390	385
9	9	658	642	650
10	10	445	432	438.5
11	11	432	420	426
12	12	626	605	615.5
13	13	260	227	243.5
14	14	477	467	472
15	15	259	268	263.5
16	16	350	370	360
17	17	451	443	447



	id	occasion	wm	mean_wm
1	1	1	512	518.5
2	1	2	525	518.5
3	2	1	430	422.5
4	2	2	415	422.5
5	3	1	520	514
6	3	2	508	514
7	4	1	428	436
8	4	2	444	436
9	5	1	500	500
10	5	2	500	500
11	6	1	600	612.5
12	6	2	625	612.5
13	7	1	364	412
14	7	2	460	412
15	8	1	380	385
16	8	2	390	385
17	9	1	658	650
18	9	2	642	650

- `xtreg` specifying level-2 variable on the fly:

```
. xtreg wm, i(id) mle
Iteration 0:   log likelihood = -187.89003
Iteration 1:   log likelihood = -184.95979
Iteration 2:   log likelihood = -184.76189
Iteration 3:   log likelihood =  -184.5855
Iteration 4:   log likelihood =  -184.5784
Iteration 5:   log likelihood = -184.57839

Random-effects ML regression                    Number of obs      =        34
Group variable: id                              Number of groups   =        17

Random effects u_i ~ Gaussian                   Obs per group: min =         2
                                                               avg =       2.0
                                                               max =         2

                                                Wald chi2(0)       =      0.00
Log likelihood  = -184.57839                    Prob > chi2        =         .

------------------------------------------------------------------------------
          wm |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |   453.9118   26.18616    17.33   0.000     402.5878    505.2357
-------------+----------------------------------------------------------------
    /sigma_u |   107.0464   18.67858                       76.0406    150.6949
    /sigma_e |   19.91083   3.414659                       14.2269     27.8656
         rho |   .9665602   .0159494                      .9210943    .9878545
------------------------------------------------------------------------------
Likelihood-ratio test of sigma_u=0: chibar2(01)=   46.27 Prob>=chibar2 = 0.000
```

- `xtreg` specifying level-2 variable at the beginning:

```
. xtset id
       panel variable:  id (balanced)
. xtreg wm, mle nolog

Random-effects ML regression                    Number of obs      =        34
Group variable: id                              Number of groups   =        17

Random effects u_i ~ Gaussian                   Obs per group: min =         2
                                                               avg =       2.0
                                                               max =         2

                                                Wald chi2(0)       =      0.00
Log likelihood  = -184.57839                    Prob > chi2        =         .

------------------------------------------------------------------------------
          wm |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
β̂      _cons |   453.9118   26.18616    17.33   0.000     402.5878    505.2357
-------------+----------------------------------------------------------------
√ψ̂  /sigma_u |   107.0464   18.67858                       76.0406    150.6949
√θ̂  /sigma_e |   19.91083   3.414659                       14.2269     27.8656
ρ̂        rho |   .9665602   .0159494                      .9210943    .9878545
------------------------------------------------------------------------------
Likelihood-ratio test of sigma_u=0: chibar2(01)=    46.27 Prob>=chibar2 = 0.000
```

$$\hat{\rho} = \frac{\hat{\psi}}{\hat{\psi}+\hat{\theta}} = \frac{107.05^2}{107.05^2+19.91^2} = 0.97$$

```
. xtmixed wm || id:, mle

Performing EM optimization:

Performing gradient-based optimization:

Iteration 0:   log likelihood = -184.57839
Iteration 1:   log likelihood = -184.57839

Computing standard errors:

Mixed-effects ML regression                     Number of obs      =        34
Group variable: id                              Number of groups   =        17

                                                Obs per group: min =         2
                                                               avg =       2.0
                                                               max =         2


                                                Wald chi2(0)       =         .
Log likelihood = -184.57839                     Prob > chi2        =         .

------------------------------------------------------------------------------
          wm |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
```

$\hat{\beta}$

```
       _cons |   453.9118   26.18617    17.33   0.000     402.5878    505.2357
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
```

$\sqrt{\hat{\psi}}$

```
                   sd(_cons) |   107.0464   18.67858      76.04062     150.695
-----------------------------+------------------------------------------------
```

$\sqrt{\hat{\theta}}$

```
                sd(Residual) |   19.91083   3.414678      14.22687    27.86564
------------------------------------------------------------------------------
LR test vs. linear regression: chibar2(01) =    46.27 Prob >= chibar2 = 0.0000
```

Inference

- We make inferences on the population mean:

$$H_0 : \beta = 0 \text{ vs } H_a : \beta \neq 0$$

$$z = \frac{\hat{\beta}}{\text{SE}(\hat{\beta})} \qquad 95\%\ \text{CI} : \hat{\beta} \pm 1.96 * SE(\hat{\beta})$$

- We can also test the between-subject variance:

$$H_0 : \psi = 0 \text{ vs } H_a : \psi > 0$$

  - whether there is significant between-subject heterogeneity
  - whether random intercept is needed (relative to linear regression)
  - can use likelihood ratio test

```
. xtreg wm, mle nolog
…
------------------------------------------------------------------------------
          wm |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |   453.9118   26.18616    17.33   0.000     402.5878    505.2357
-------------+----------------------------------------------------------------
    /sigma_u |   107.0464   18.67858                       76.0406    150.6949
    /sigma_e |   19.91083   3.414659                       14.2269     27.8656
         rho |   .9665602   .0159494                      .9210943    .9878545
------------------------------------------------------------------------------
Likelihood-ratio test of sigma_u=0: chibar2(01)=    46.27 Prob>=chibar2 = 0.000
```

$$H_0 : \beta = 0$$

```
. xtmixed wm || id:, mle
…
------------------------------------------------------------------------------
          wm |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       _cons |   453.9118   26.18617    17.33   0.000     402.5878    505.2357
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
                   sd(_cons) |   107.0464   18.67858      76.04062     150.695
-----------------------------+------------------------------------------------
                sd(Residual) |   19.91083   3.414678      14.22687    27.86564
------------------------------------------------------------------------------
LR test vs. linear regression: chibar2(01) =    46.27 Prob >= chibar2 = 0.0000
```

$$H_0 : \psi = 0$$

- equivalent to fitting reduced and full model then using the `lrtest` command.
  - because of the constraint $\psi \geq 0$, the p-value has to be divided by 2.

```
. estimates store ri
. quietly xtmixed wm, mle
. lrtest ri

Likelihood-ratio test                                 LR chi2(1)  =     46.27
(Assumption: . nested in ri)                          Prob > chi2 =    0.0000
```

Need to divide by 2

Fixed vs Random Effects

- In the PEFR example, we could have treated the subject effects as a fixed factor in an ANOVA model (or as a bunch of dummy variables in a regression model). This is known as a fixed effects model.
- Both the random intercept model and fixed effects model include subject-specific intercepts (level-2) to account for unobserved heterogeneity

Fixed vs Random Effects…

- Which model should be used?
  - If the target of inference is on the population of subjects/groups, then the effect should be random.
  - If the target of inference is on the subjects/groups in the particular sample, then the effect should be fixed.

Fixed vs Random Effects…

- Notes on random effects:
  - assume cluster effects is exchangeable, i.e., at the same *level*
  - need enough clusters (>10)
  - cluster size at least 2 (but singletons also used but don't contribute to estimating within-cluster correlation)

Clustered data example (GSCE)

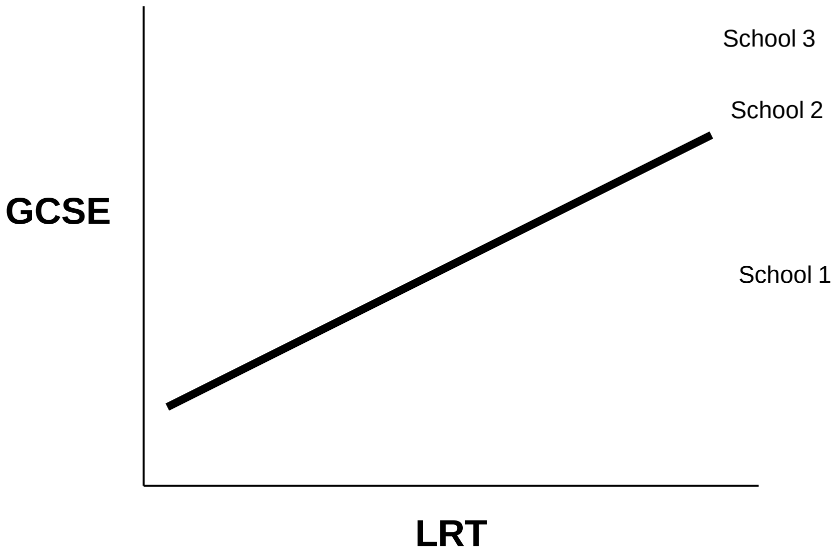
- Cross-sectional data:
  - Level-1 unit: student
  - Level-2 unit: school

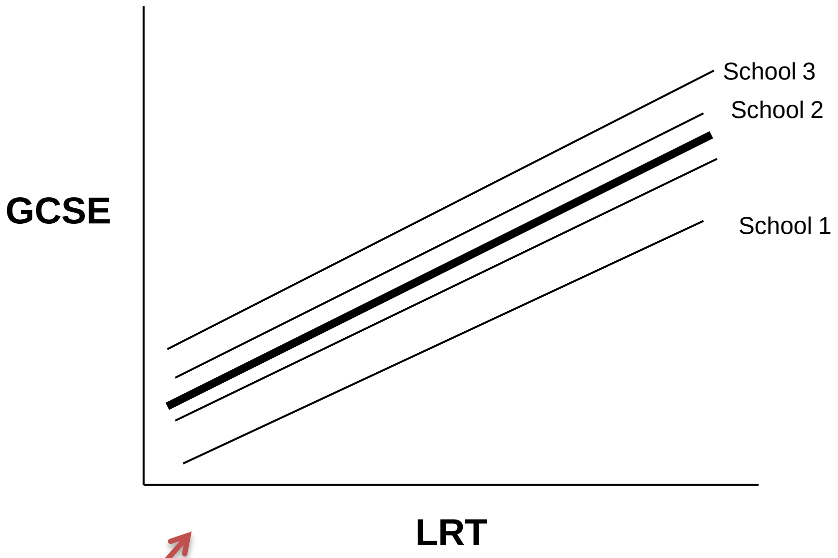
Models

- Random Intercept model
  - overall level of response vary between clusters
- Random Intercept model with covariates
  - overall level of response vary between clusters
  - covariate effects common across clusters
- Random Coefficient model (with covariate)
  - overall level of response vary between clusters
  - covariate effects vary between clusters

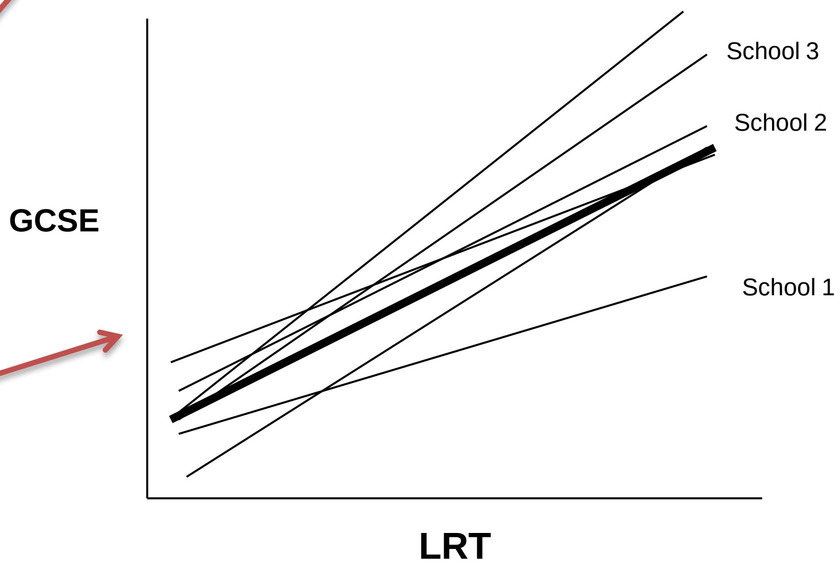
GCSE Example

- How effective are different schools?
  - Outcome: Graduate Certificate of Secondary Education (GCSE) – taken at age 16
  - Sample: ~4000 students within 65 schools
  - Primary covariate: London Reading test (LRT) – taken at age 11
  - Other covariates: gender, school type
- Research question:
  - Effect of LRT on GCSE?
  - Does it vary among schools?

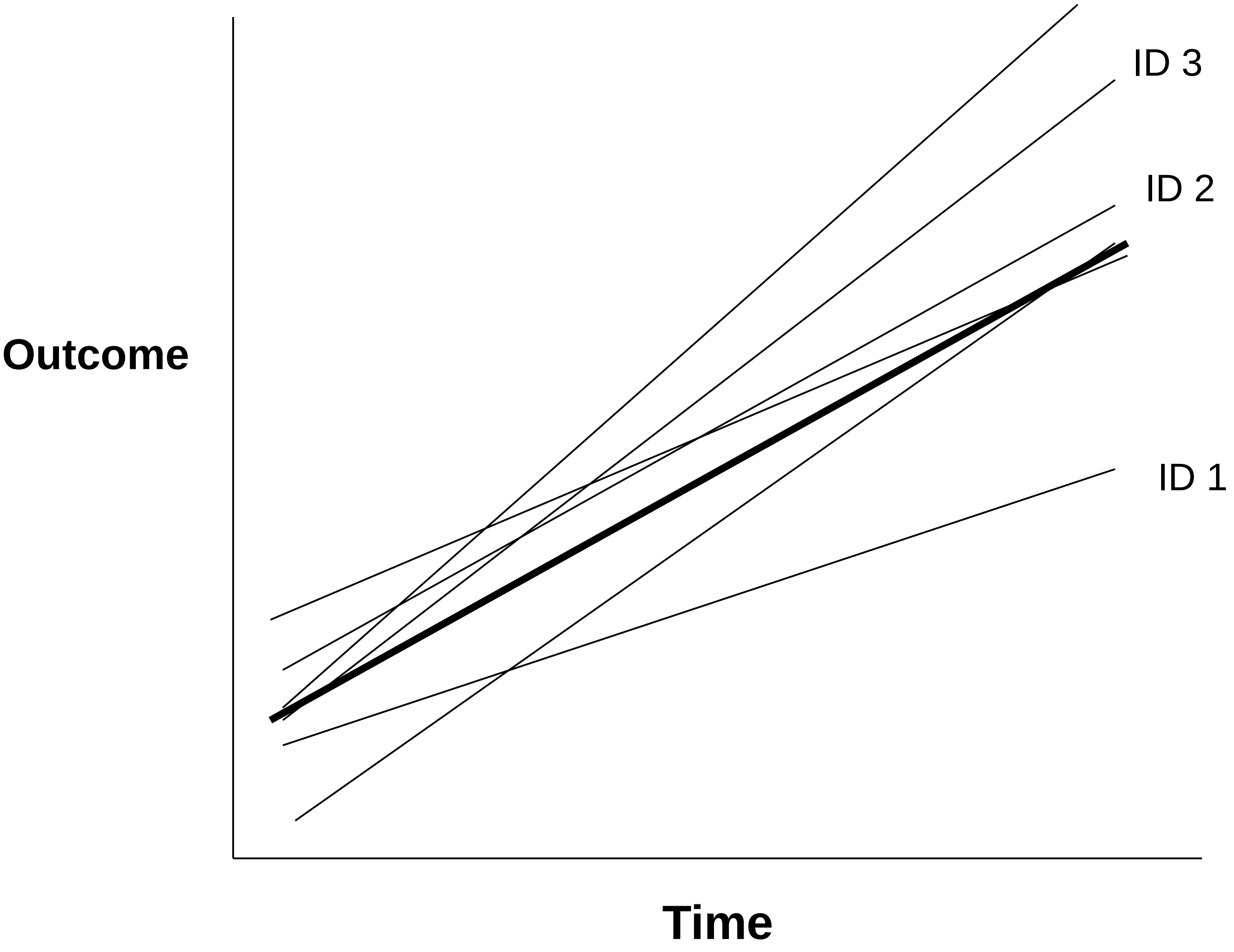




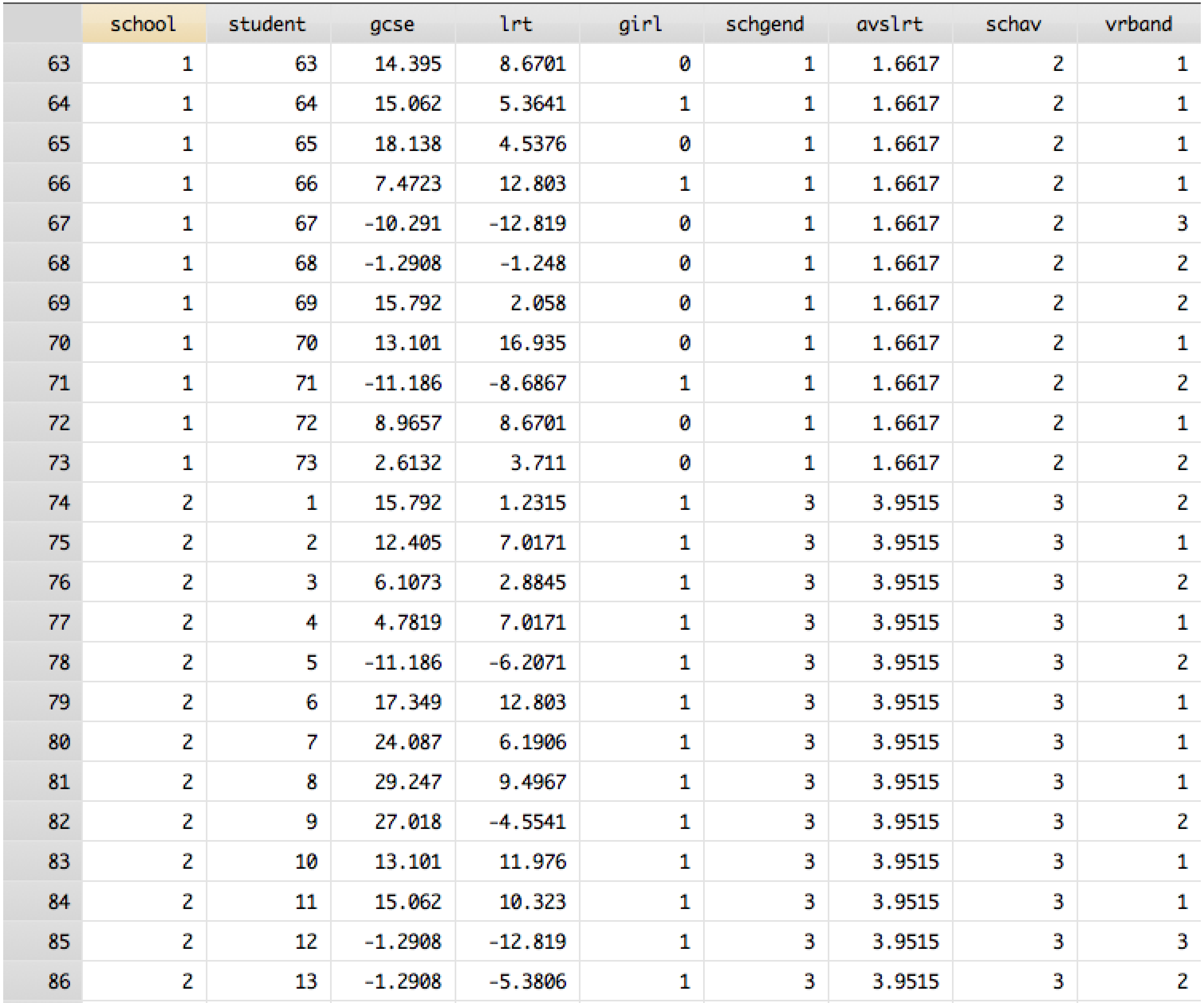
- Linear regression
- Random intercept
- Random Coefficient



- Longitudinal data



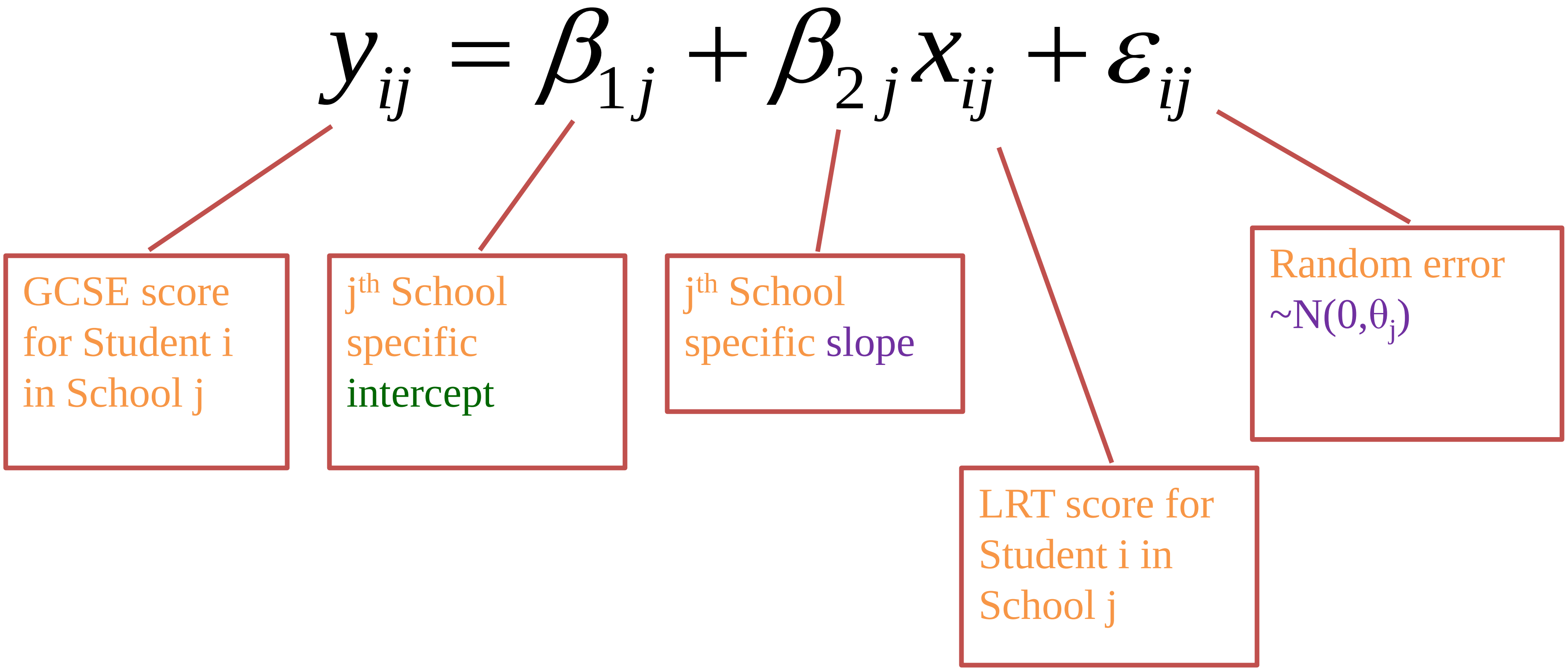
GCSE Data



	school	student	gcse	lrt	girl	schgend	avslrt	schav	vrband
63	1	63	14.395	8.6701	0	1	1.6617	2	1
64	1	64	15.062	5.3641	1	1	1.6617	2	1
65	1	65	18.138	4.5376	0	1	1.6617	2	1
66	1	66	7.4723	12.803	1	1	1.6617	2	1
67	1	67	-10.291	-12.819	0	1	1.6617	2	3
68	1	68	-1.2908	-1.248	0	1	1.6617	2	2
69	1	69	15.792	2.058	0	1	1.6617	2	2
70	1	70	13.101	16.935	0	1	1.6617	2	1
71	1	71	-11.186	-8.6867	1	1	1.6617	2	2
72	1	72	8.9657	8.6701	0	1	1.6617	2	1
73	1	73	2.6132	3.711	0	1	1.6617	2	2
74	2	1	15.792	1.2315	1	3	3.9515	3	2
75	2	2	12.405	7.0171	1	3	3.9515	3	1
76	2	3	6.1073	2.8845	1	3	3.9515	3	2
77	2	4	4.7819	7.0171	1	3	3.9515	3	1
78	2	5	-11.186	-6.2071	1	3	3.9515	3	2
79	2	6	17.349	12.803	1	3	3.9515	3	1
80	2	7	24.087	6.1906	1	3	3.9515	3	1
81	2	8	29.247	9.4967	1	3	3.9515	3	1
82	2	9	27.018	-4.5541	1	3	3.9515	3	2
83	2	10	13.101	11.976	1	3	3.9515	3	1
84	2	11	15.062	10.323	1	3	3.9515	3	1
85	2	12	-1.2908	-12.819	1	3	3.9515	3	3
86	2	13	-1.2908	-5.3806	1	3	3.9515	3	2

Can we fit a separate regression line within each school?

Separate Linear Regression for each School



$$y_{ij} = \beta_{1j} + \beta_{2j} x_{ij} + \varepsilon_{ij}$$

GCSE score for Student i in School j

jth School specific intercept

jth School specific slope

LRT score for Student i in School j

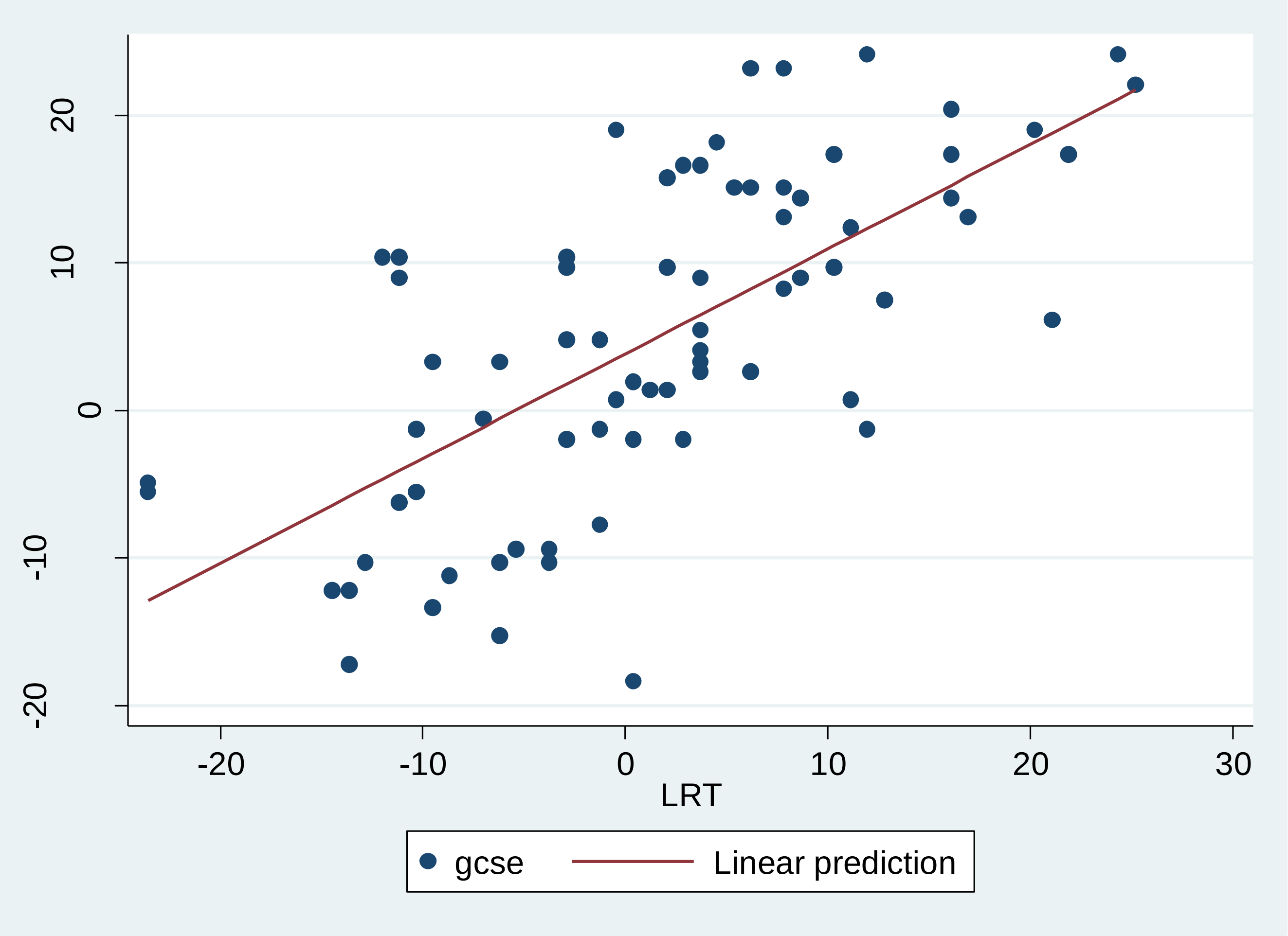
Random error $\sim N(0,\theta_j)$

- Fit a regression line for school 1:

```
. use http://www.stata-press.com/data/mlmus3/gcse
. regress gcse lrt if school==1

      Source |       SS       df       MS              Number of obs =      73
-------------+------------------------------           F(  1,    71) =   59.44
       Model |  4084.89189     1  4084.89189           Prob > F      =  0.0000
    Residual |  4879.35759    71  68.7233463           R-squared     =  0.4557
-------------+------------------------------           Adj R-squared =  0.4480
       Total |  8964.24948    72  124.503465           Root MSE      =    8.29

------------------------------------------------------------------------------
        gcse |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lrt |   .7093406   .0920061     7.71   0.000     .5258856    .8927955
       _cons |   3.833302   .9822377     3.90   0.000     1.874776    5.791828
------------------------------------------------------------------------------
```

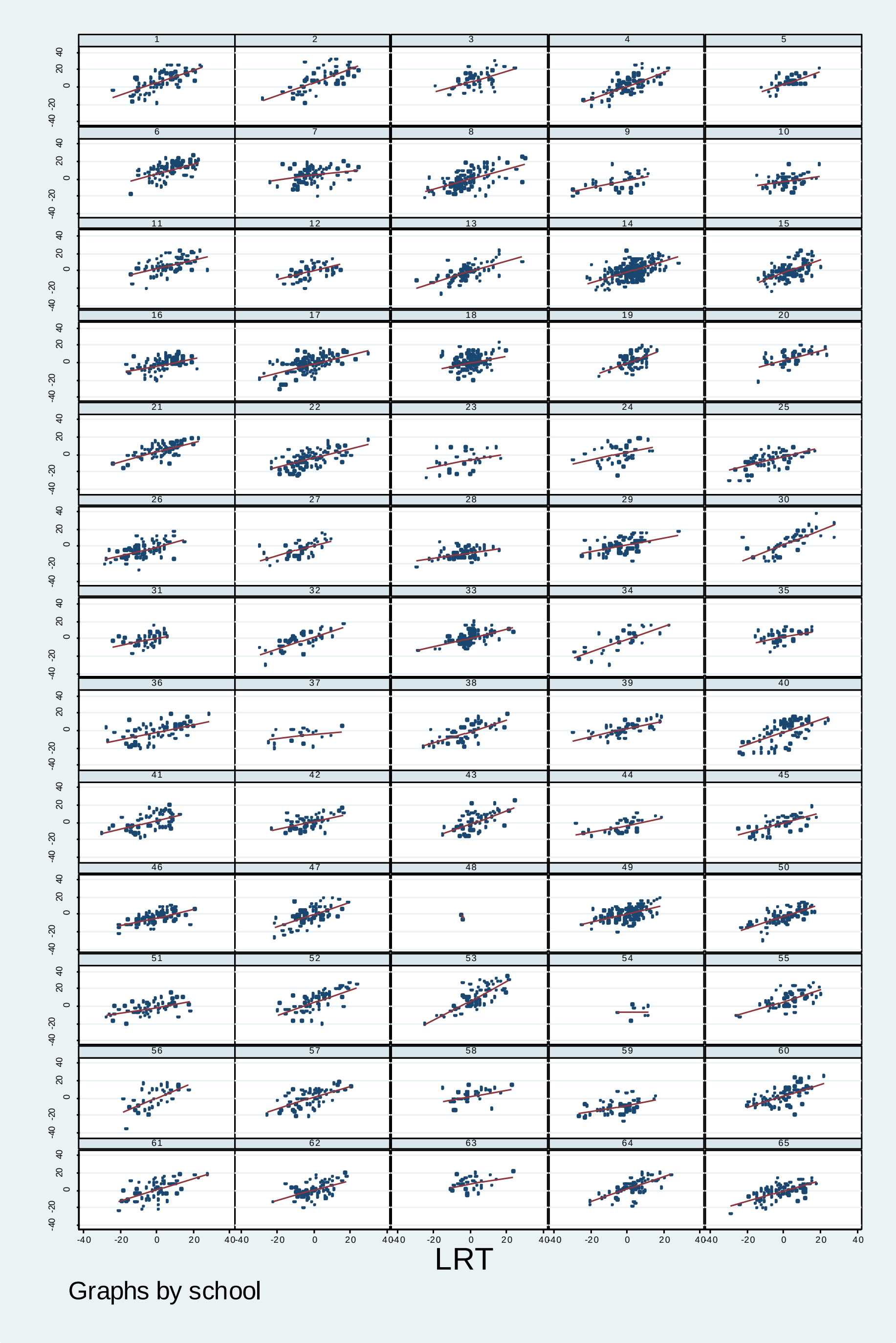
- Fitted regression line for school 1:

```
. predict p_gcse, xb
. twoway (scatter gcse lrt) (line p_gcse lrt, sort) if school==1, xtitle(LRT)
  ytitle(GCSE)
```



- To obtain a trellis graph containing such plots for all 65 school:

```
. twoway(scatter gcse lrt) (lfit
  gcse lrt, sort lpatt(solid)),
  by(school, compact
  legend(off) cols(5))
  xtitle(LRT) ytitle(GCSE)
  ysize(3) xsize(2)
```



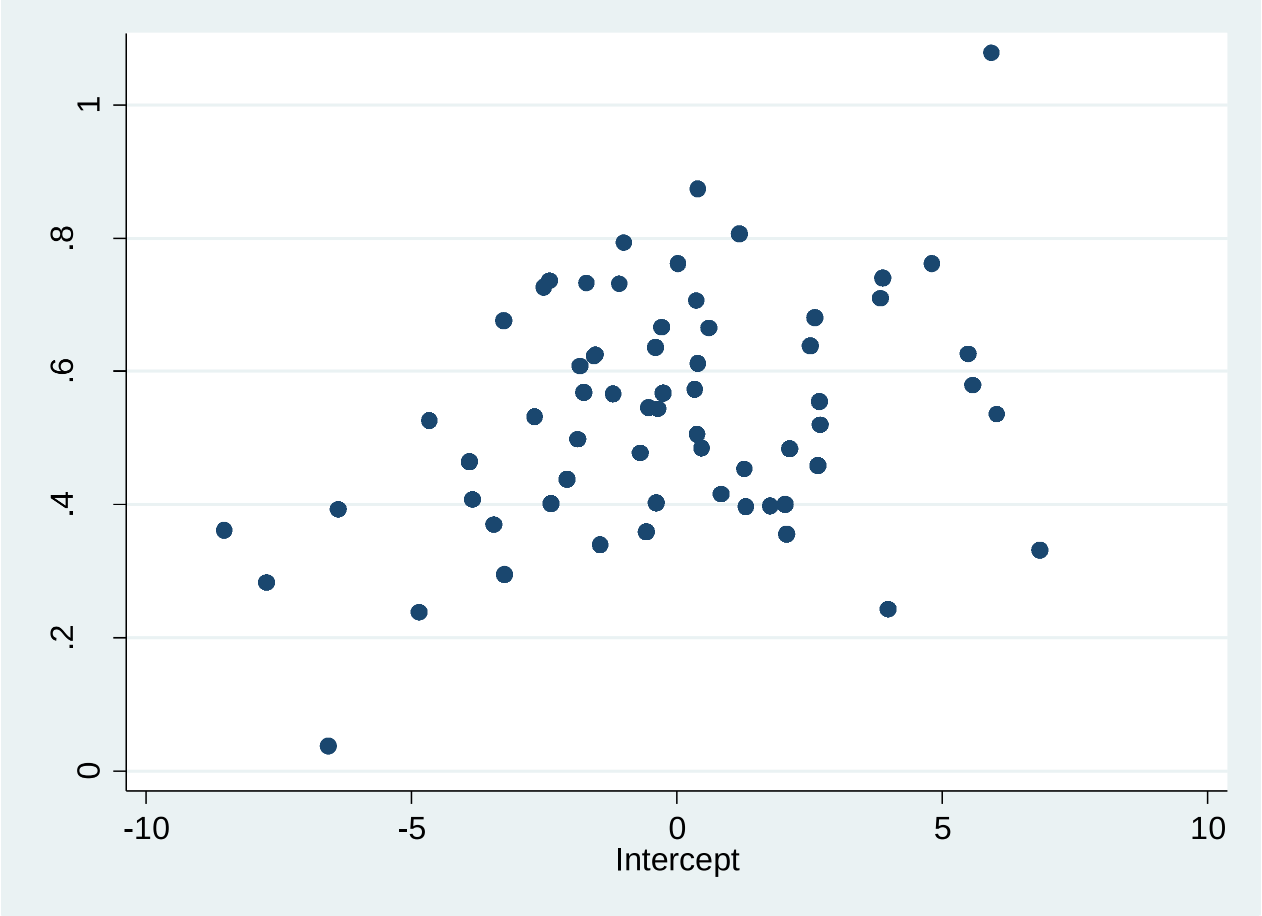
Separate Linear Regression for each School

- We will now fit a SLRM for each school and summarize the estimates across schools:
    1. Estimate slope and intercept for each school
    2. Estimate the mean slope and mean intercept
    3. Estimate variance and covariance (also correlation) for slopes and intercepts

- Stata code

```
. egen num=count(gcse),by (school)
. statsby inter=_b[_cons] slope=_b[lrt],by(school) saving(ols): regress gcse lrt if num>4
(running regress on estimation sample)

      command:  regress gcse lrt if num>4
        inter:  _b[_cons]
        slope:  _b[lrt]
           by:  school

Statsby groups
----+--- 1 ---+--- 2 ---+--- 3 ---+--- 4 ---+--- 5
..................................................    50
..............

. sort school
. merge m:1 school using ols
    Result                           # of obs.
    -----------------------------------------
    not matched                             2
        from master                         2  (_merge==1)
        from using                          0  (_merge==2)

    matched                             4,057  (_merge==3)
    -----------------------------------------
. drop _merge
. twoway scatter slope inter, xtitle(Intercept) ytitle(Slope)
```

- Scatter plot of fitted slopes and intercepts

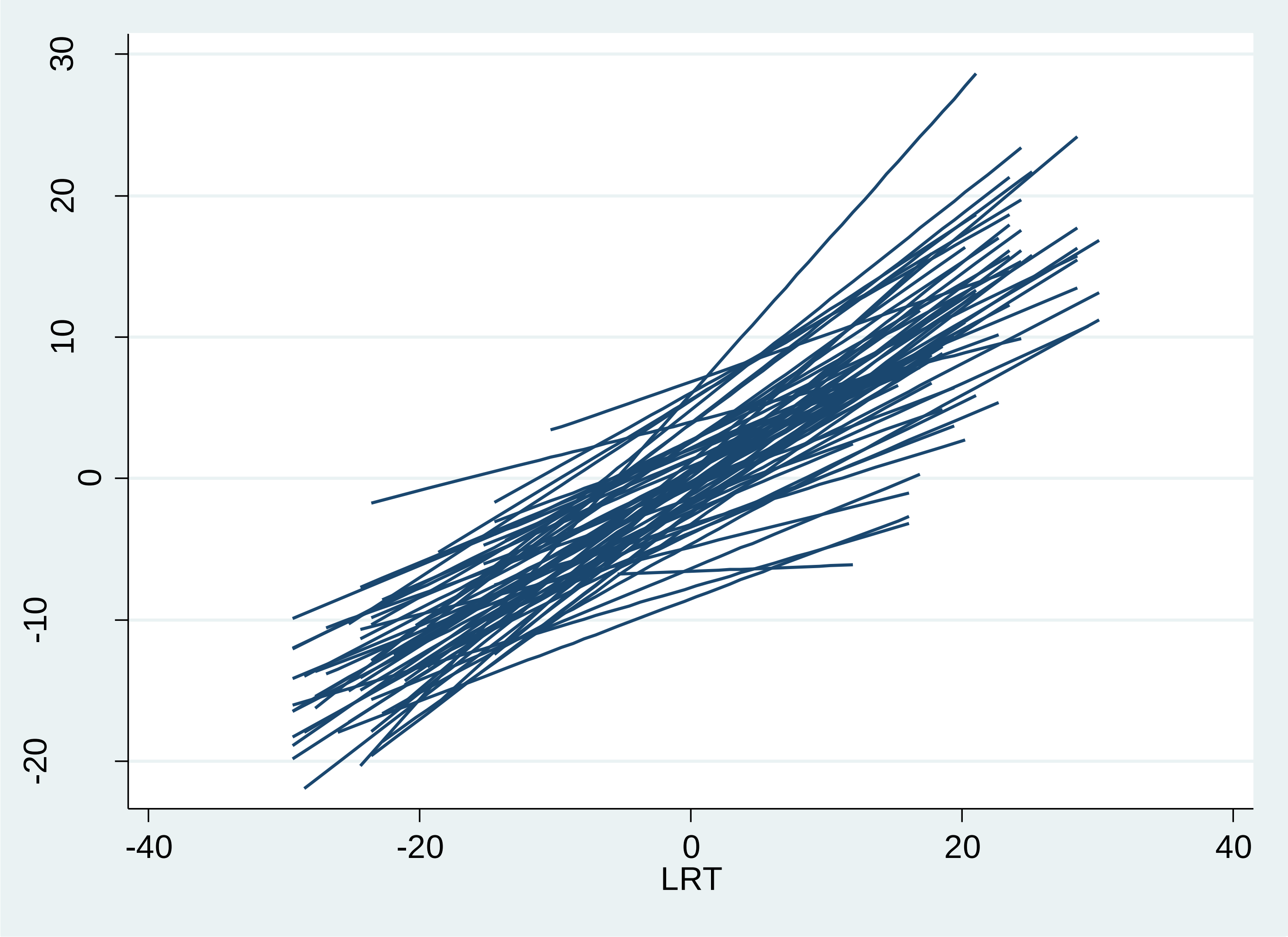


- Do the intercepts vary across schools?
- Do the slopes vary across schools?
- Is there a relationship between the intercepts and slopes?

Spaghetti Plot:

```
. generate pred=inter+slope*lrt
(2 missing values generated)
. sort school lrt
. twoway (line pred lrt, connect(ascending)), xtitle(LRT) ytitle(Fitted
   regression lines)
```

calculate predicted values



- Do the intercepts vary across schools?
- Do the slopes vary across schools?

Creating a Joint Model

- Approach 1: dummy variable for each school
  - assumes common residual variance ($\theta_j = \theta$)
  - need interaction of each dummy variable with LRT (how many?!)
  - assumes fixed school effect (inference limited to schools in the sample)

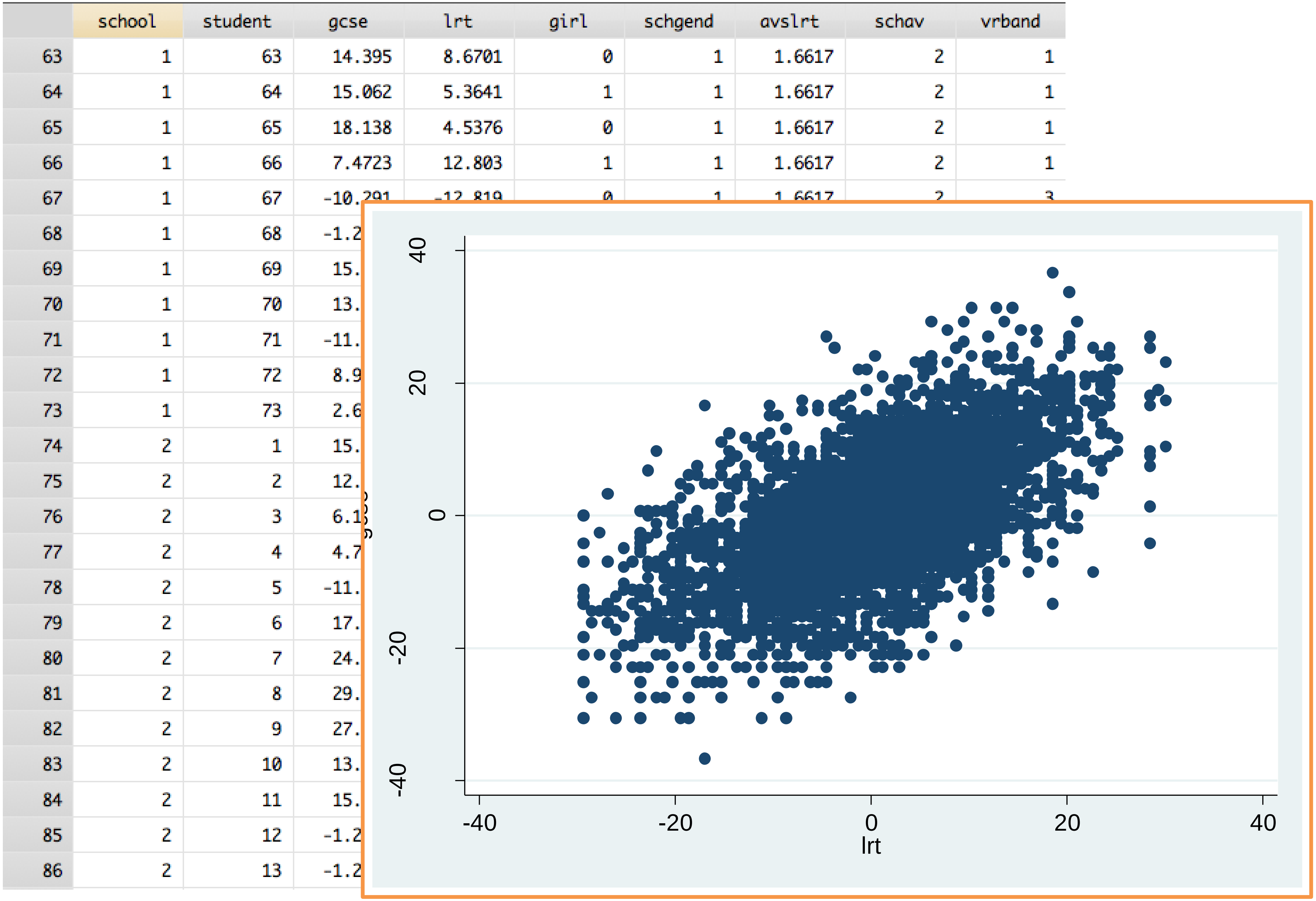
Creating a Joint Model

- Better approach: Random Coefficient model
  - school-specific intercept, school-specific slope
  - estimate mean intercept and mean slope
  - describe (co)variation in intercepts and slopes

Estimation using Stata

- We can use `xtmixed` to fit random coefficient models
  - `xtreg` can only fit 2-level random intercept models
- Recall: want to model GCSE as a function of LRT

GCSE Data



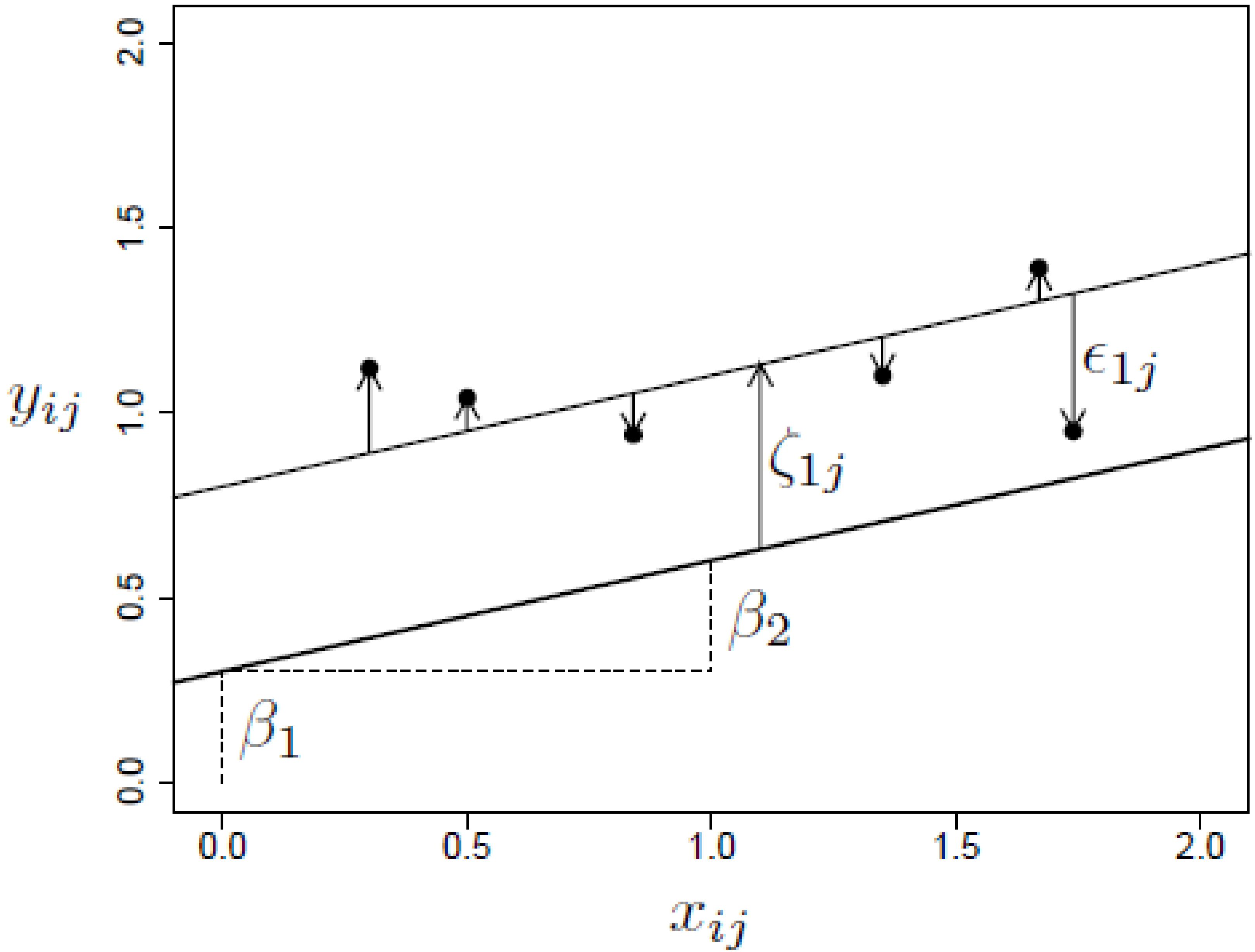
	school	student	gcse	lrt	girl	schgend	avslrt	schav	vrband
63	1	63	14.395	8.6701	0	1	1.6617	2	1
64	1	64	15.062	5.3641	1	1	1.6617	2	1
65	1	65	18.138	4.5376	0	1	1.6617	2	1
66	1	66	7.4723	12.803	1	1	1.6617	2	1
67	1	67	-10.291	-12.819	0	1	1.6617	2	3
68	1	68	-1.2						
69	1	69	15.						
70	1	70	13.						
71	1	71	-11.						
72	1	72	8.9						
73	1	73	2.6						
74	2	1	15.						
75	2	2	12.						
76	2	3	6.1						
77	2	4	4.7						
78	2	5	-11.						
79	2	6	17.						
80	2	7	24.						
81	2	8	29.						
82	2	9	27.						
83	2	10	13.						
84	2	11	15.						
85	2	12	-1.2						
86	2	13	-1.2						

Random Intercept (RI) Model

- First we fit an RI model
  - subject-specific intercept
  - common LRT slope across schools
    - Var(Slope) = $\psi_{22} = 0$
    - Cov(Int,Slope) = $\psi_{12} = 0$

$$GCSE_{ij} = \beta_1 + \beta_2 * LRT_{ij} + \zeta_{1j} + \varepsilon_{ij}$$

Random-intercept model



```
. xtmixed gcse lrt || school:, mle nolog

Mixed-effects ML regression                     Number of obs      =      4059
Group variable: school                          Number of groups   =        65

                                                Obs per group: min =         2
                                                               avg =      62.4
                                                               max =       198


                                                Wald chi2(1)       =   2042.57
Log likelihood = -14024.799                     Prob > chi2        =    0.0000

------------------------------------------------------------------------------
        gcse |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         lrt |   .5633697   .0124654    45.19   0.000     .5389381    .5878014
       _cons |   .0238706   .4002255     0.06   0.952     -.760557    .8082982
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
school: Identity             |
                   sd(_cons) |   3.035269   .3052513      2.492261    3.696587
-----------------------------+------------------------------------------------
                sd(Residual) |   7.521481   .0841759      7.358295    7.688285
------------------------------------------------------------------------------
LR test vs. linear regression: chibar2(01) =   403.27 Prob >= chibar2 = 0.0000

. estimates store ri
```

$\hat{\beta}_2$

$\hat{\beta}_1$

$\sqrt{\hat{\psi}_{11}}$

$\sqrt{\hat{\theta}}$

Is there an LRT effect?

$$H_0 : \beta_2 = 0 \text{ vs } H_a : \beta_2 \neq 0$$

Conclusion:

- z = 0.5634/0.01247 = 45.19
- p-value <0.001
- LRT is significantly associated with GCSE

95% CI for LRT effect?

$$\hat{\beta}_2 \pm 1.96 * \text{SE}\left(\hat{\beta}_2\right)$$

$$= (0.54, 0.59)$$

Calculate the ICC:

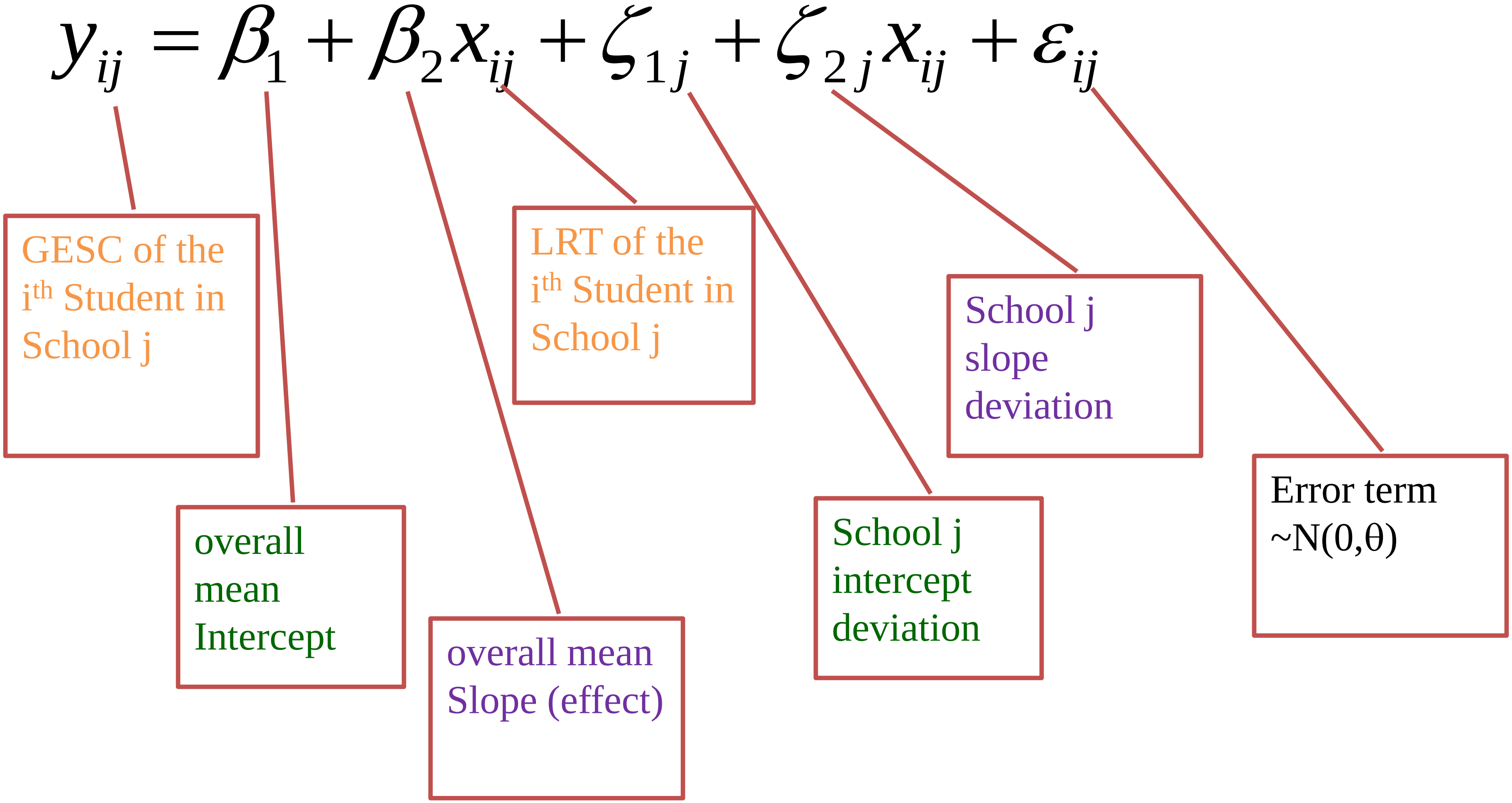
$$\hat{\rho} = \frac{\widehat{\psi}_{11}}{\widehat{\psi}_{11} + \hat{\theta}} = \frac{3.035^2}{3.035^2 + 7.521^2} = 0.14$$

Interpretation:

- Proportion of total variance in GCSE due to school-to-school variation is 14%
- Within-school correlation is relatively low

Random Coefficient Model

Model:



$$y_{ij} = \beta_1 + \beta_2 x_{ij} + \zeta_{1j} + \zeta_{2j} x_{ij} + \varepsilon_{ij}$$

GESC of the ith Student in School j

overall mean Intercept

overall mean Slope (effect)

LRT of the ith Student in School j

School j intercept deviation

School j slope deviation

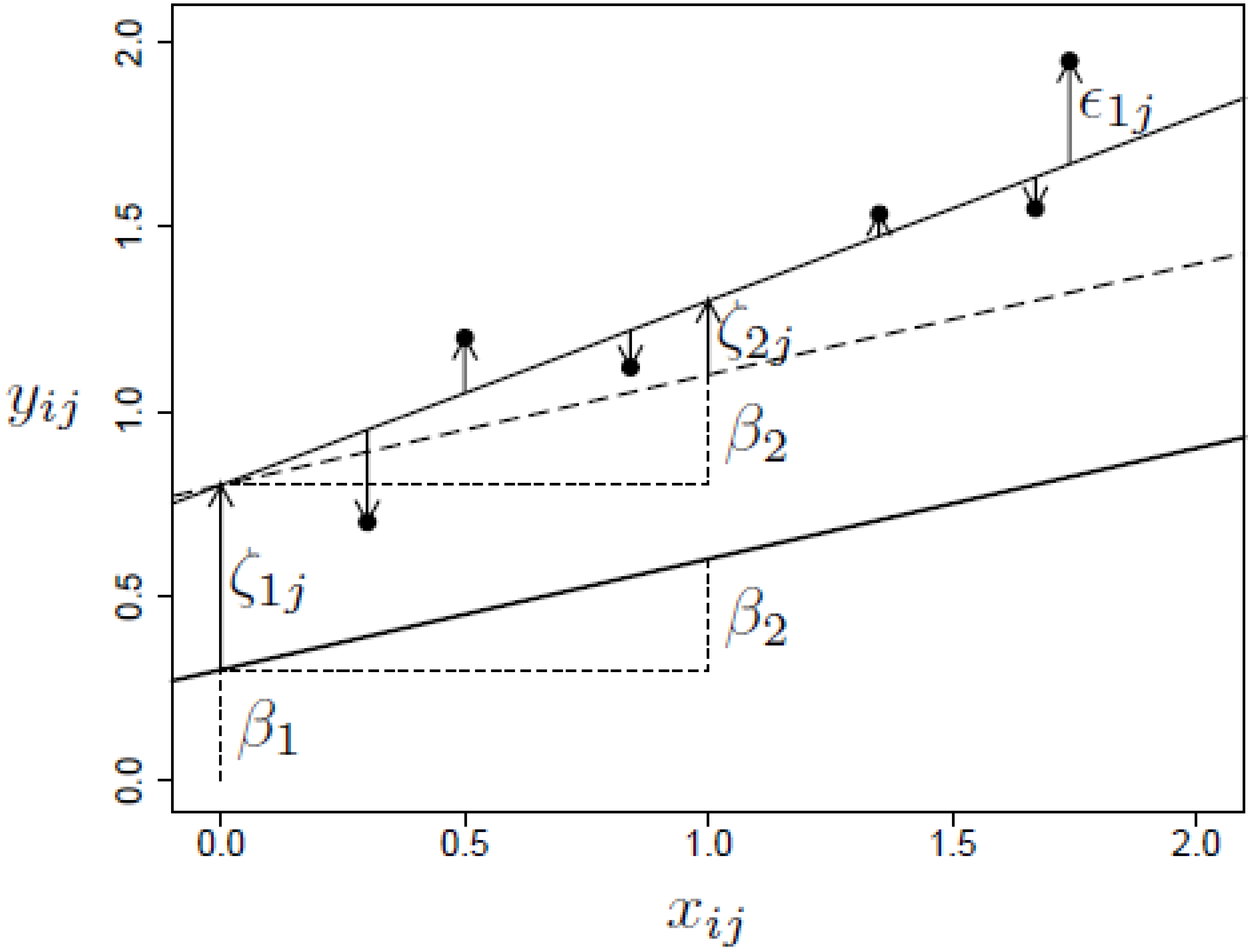
Error term ~N(0,θ)

Random Coefficient (RC) Model

- Next we fit an RC model
  - – subject-specific intercept
  - – subject-specific slope
  - – possible intercept-slope covariance

$$GCSE_{ij} = \beta_1 + \beta_2 * LRT_{ij} + \zeta_{1j} + \zeta_{2j} * LRT_{ij} + \varepsilon_{ij}$$

Random-coefficient model



```
. xtmixed gcse lrt || school:lrt, cov(unstructured) mle nolog
```

slope

ψ_{12}

```
Mixed-effects ML regression                     Number of obs      =      4059
Group variable: school                          Number of groups   =        65

                                                Obs per group: min =         2
                                                               avg =      62.4
                                                               max =       198


                                                Wald chi2(1)       =    779.79
Log likelihood = -14004.613                     Prob > chi2        =    0.0000

------------------------------------------------------------------------------
        gcse |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
```

$\hat{\beta}_2$

$\hat{\beta}_1$

```
         lrt |    .556729   .0199368    27.92   0.000     .5176535    .5958044
       _cons |   -.115085   .3978346    -0.29   0.772    -.8948264    .6646564
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
school: Unstructured         |
```

$\sqrt{\hat{\psi}_{22}}$

$\sqrt{\hat{\psi}_{11}}$

$\hat{\rho}_{12}$

```
                    sd(lrt) |   .1205646   .0189827      .0885522    .1641498
                  sd(_cons) |   3.007444   .3044148      2.466258    3.667385
            corr(lrt,_cons) |   .4975415   .1487427      .1572768    .7322094
-----------------------------+------------------------------------------------
```

$\sqrt{\hat{\theta}}$

```
               sd(Residual) |   7.440787   .0839482      7.278058    7.607155
------------------------------------------------------------------------------
LR test vs. linear regression:       chi2(3) =   443.64   Prob > chi2 = 0.0000

Note: LR test is conservative and provided only for reference.

. estimates store rc
```

Estimated Covariance and Correlation:

```
. estat recovariance
Random-effects covariance matrix for level school

             |       lrt      _cons
-------------+----------------------
         lrt |   .0145358
       _cons |   .1804042    9.04472
```

$$\hat{\rho}_{12} = \frac{\widehat{\psi}_{21}}{\sqrt{\widehat{\psi}_{11}\widehat{\psi}_{22}}} = \frac{0.18}{\sqrt{0.0145 * 9.044}} = 0.50$$

Interpretation:

- LRT tends to have greater effect (slope) in schools with higher school-specific GCSE (intercept)

Does the RC model fit better than the RI model?

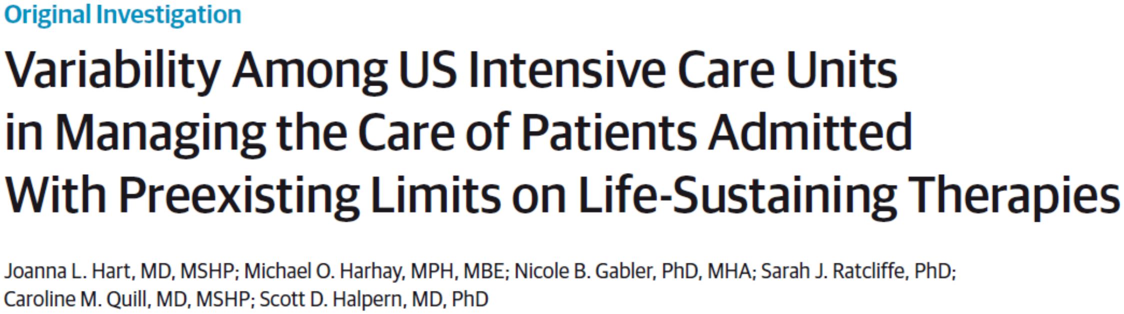
- Test the slope variance:

$$H_0 : \psi_{22} = 0 \qquad H_a : \psi_{22} > 0$$

```
. lrtest rc ri

Likelihood-ratio test                                 LR chi2(2)  =     40.37
(Assumption: ri nested in rc)                         Prob > chi2 =    0.0000

Note: The reported degrees of freedom assumes the null hypothesis is not on
      the boundary of the parameter space.  If this is not true, then the
      reported test is conservative.
```

Need to divide by 2 to get correct p-value

Examples

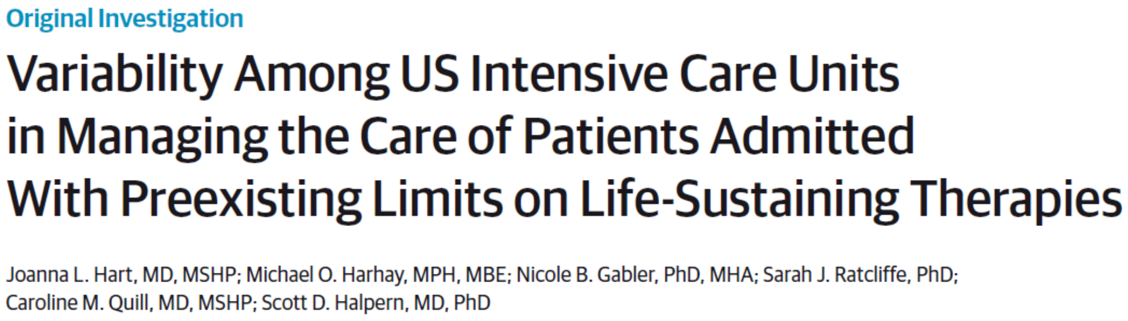


Original Investigation

Variability Among US Intensive Care Units in Managing the Care of Patients Admitted With Preexisting Limits on Life-Sustaining Therapies

Joanna L. Hart, MD, MSHP; Michael O. Harhay, MPH, MBE; Nicole B. Gabler, PhD, MHA; Sarah J. Ratcliffe, PhD;
Caroline M. Quill, MD, MSHP; Scott D. Halpern, MD, PhD

- Retrospective cohort using Project IMPACT
- 277,693 patient visits in 141 ICUs in 105 hospitals
- Explored ICU- and patient-level associations with admission of patients with preexisting treatment limitations



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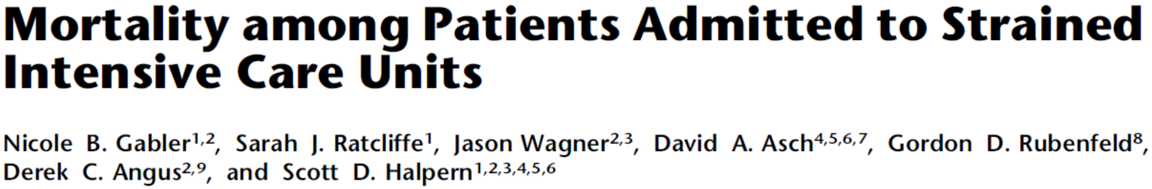
- Two illustrative analyses:
  - (1) Fixed effect models that did and did not include ICU as a fixed effect to explore the association of patient race (white / black / other) with the outcome
  - (2) Random effect models that did and did not include ICU as a random effect to explore the association of race and ICU model (open / closed) with the outcome

ICU as a fixed effect – patient level

	With ICU as a fixed effect	Without ICU as a fixed effect
Race (ref=White)	OR (95% CI)	OR (95% CI)
Black	0.55 (0.51, 0.59)	0.47 (0.44, 0.50)
Other	0.56 (0.51. 0.60)	0.64 (0.59, 0.68)
Race (ref=White)	Beta (SE)	Beta (SE)
Black	-0.60 (0.036)	-0.75 (0.032)
Other	-0.59 (0.041)	-0.45 (0.036)

ICU as a random effect – patient and ICU level

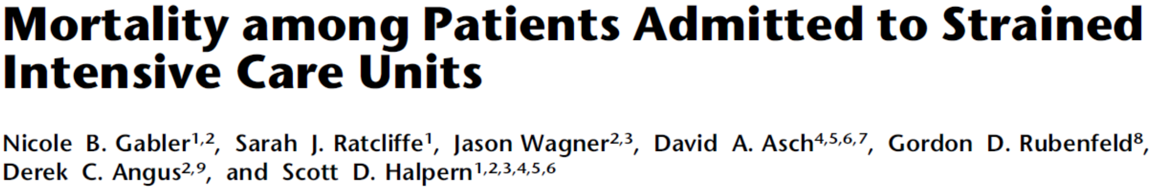
	With ICU as a fixed effect	Without ICU as a fixed effect
Race (ref=White)	OR (95% CI)	OR (95% CI)
Black	0.55 (0.51, 0.58)	0.47 (0.44, 0.50)
Other	0.56 (0.52, 0.60)	0.63 (0.59, 0.68)
Model (ref=Open)		
Closed	1.07 (0.76, 1.51)	0.81 (0.75, 0.87)
Race (ref=White)	Beta (SE)	Beta (SE)
Black	-0.61 (0.035)	-0.76 (0.033)
Other	-0.58 (0.040)	0.46 (0.036)
Model (ref=Open)		
Closed	0.069 (0.177)	-0.22 (0.037)



Mortality among Patients Admitted to Strained Intensive Care Units

Nicole B. Gabler[1,2], Sarah J. Ratcliffe[1], Jason Wagner[2,3], David A. Asch[4,5,6,7], Gordon D. Rubenfeld[8], Derek C. Angus[2,9], and Scott D. Halpern[1,2,3,4,5,6]

- Retrospective cohort using Project IMPACT
- 264,401 patient visits in 155 ICUs in 107 hospitals over 8 years (total of 658 ICU-years)
- Explored the association between ICU strain (census, acuity of other ICU patients, number of new admissions) and in-hospital mortality



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- Multiple ways to cluster: Hospital? ICU? Year? ICU and year? ICU-year? Etc..
- Random or fixed effect?
- Cannot cluster on hospital and ICU because most hospitals only have a single ICU
- We chose to model ICU as a fixed effect to control for known differences across ICUs
- ICU and year entered as single term; if ICU-specific effects change over time, we did not want to assume the changes are in the same direction

Clustering on ICU and year

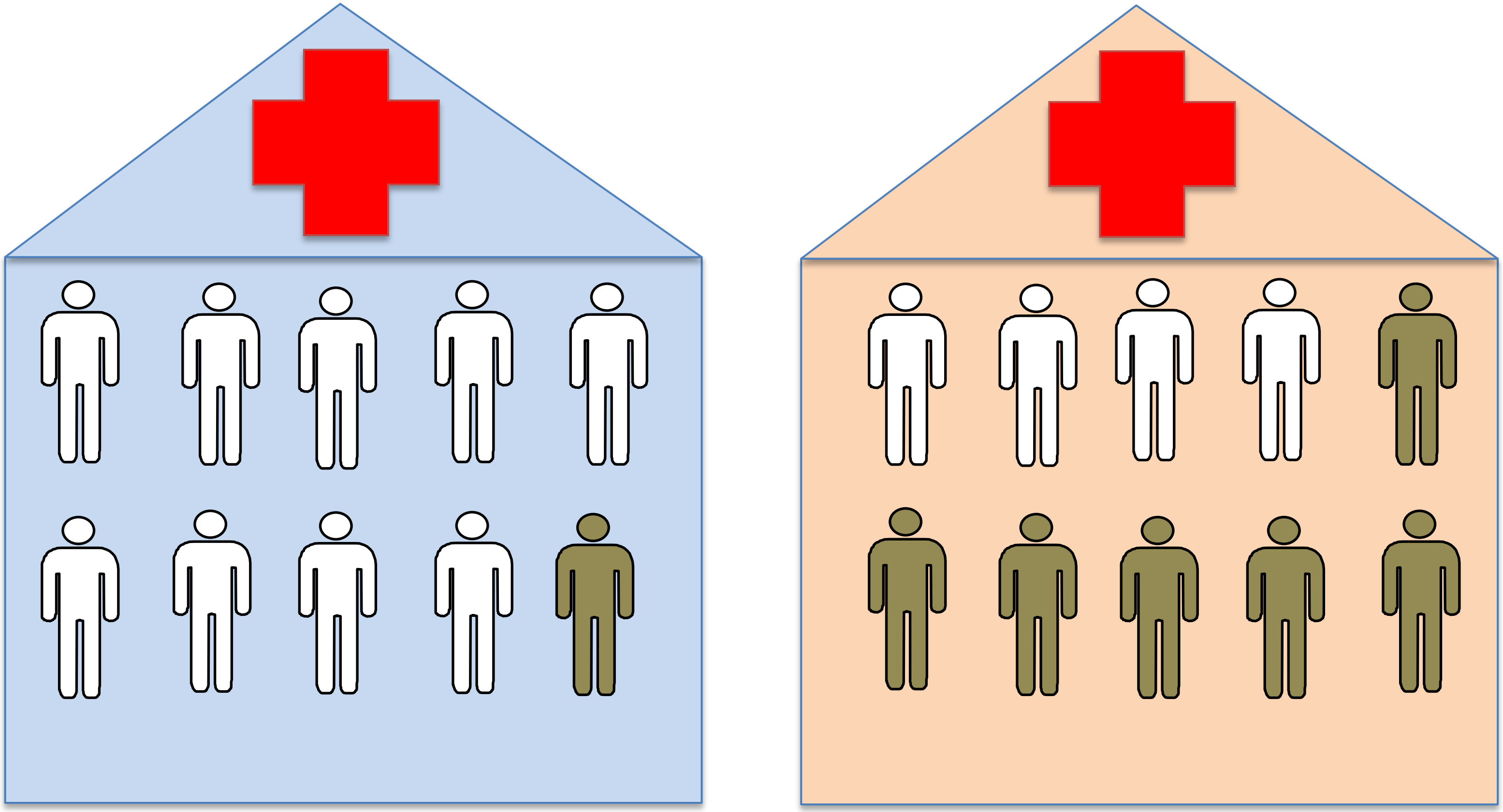
	ICU-year entered as a single term	ICU and year entered separately
	OR (95% CI)	OR (95% CI)
Census	1.011 (0.996, 1.025)	1.011 (0.996, 1.025)
Acuity	0.998 (0.977, 1.019)	0.958 (0.937, 0.977)
Admissions	0.970 (0.957, 0.983)	0.967 (0.954, 0.979)
	Beta (SE)	Beta (SE)
Census	0.011 (0.007)	0.011 (0.007)
Acuity	-0.002 (0.011)	-0.043 (0.010)
Admissions	-0.031 (0.007)	-0.034 (0.007)

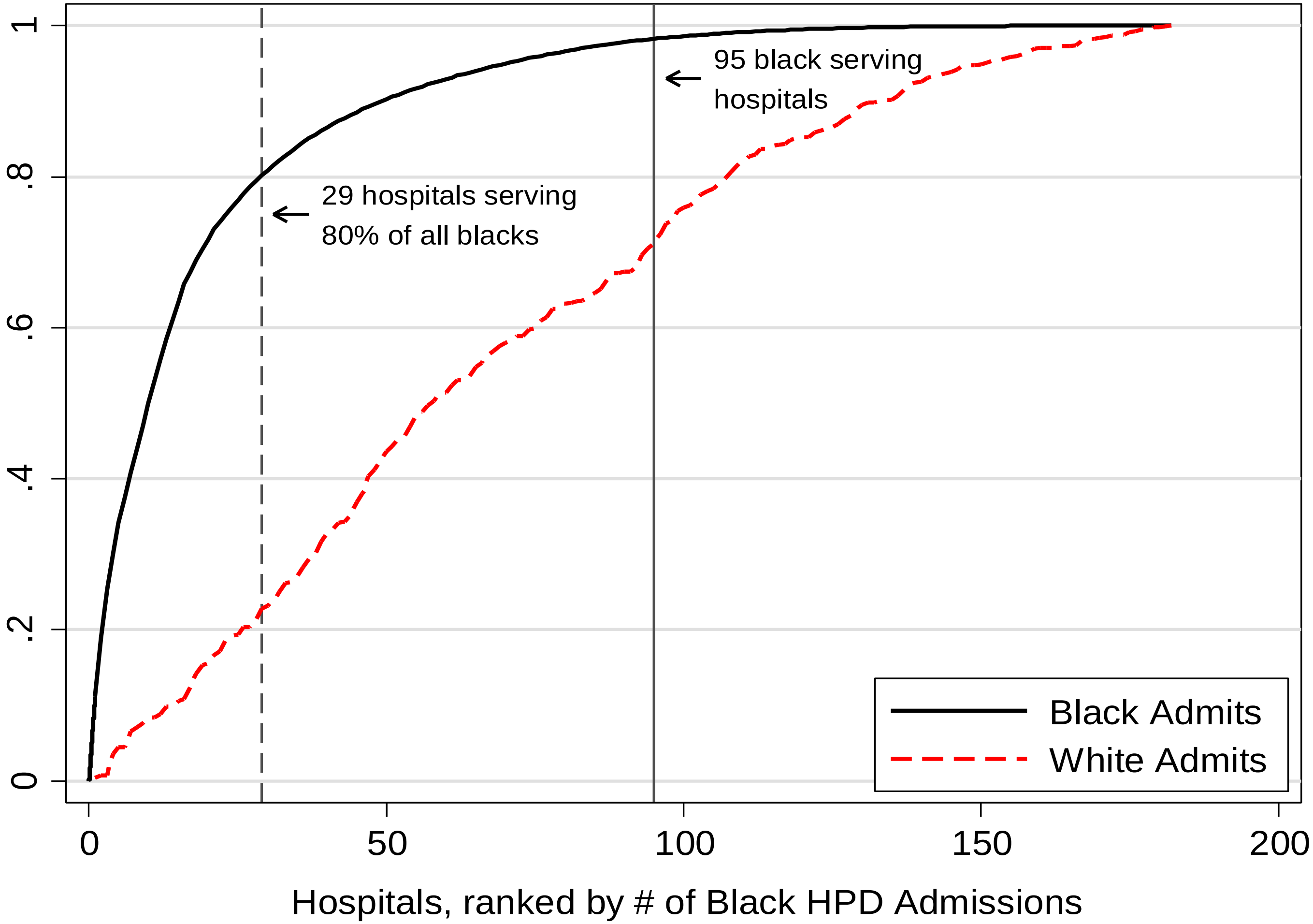
Final thoughts

- Clustering should be considered any time study participants can be contained within groups
- Failing to do so may result in incorrect estimates, confidence intervals, and p-values
- Fixed effects, random effects, and use of cluster/robust error terms are all ways to handle clustering
- The choice of the clustering variable depends on the data and your research question

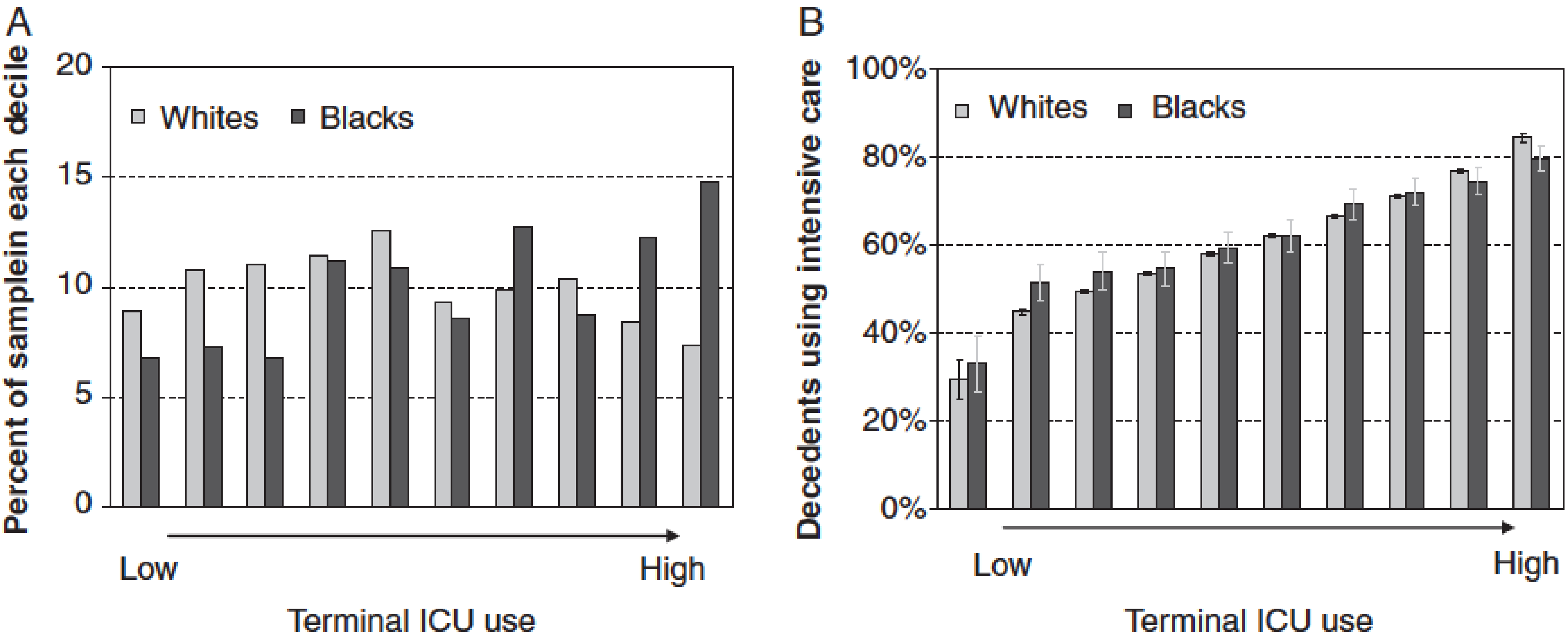
Racial disparities

- Blacks and whites tend to live in segregated regions and use different hospitals
- If these hospitals differ in treatment patterns, some of the observed racial disparities may be mediated by a hospital effect rather than by race.
  - How does this affect policy implications of findings?





1
.8
.6
.4
.2
0
0
50
100
150
200
Hospitals, ranked by # of Black HPD Admissions
29 hospitals serving
80% of all blacks
95 black serving
hospitals
Black Admits
White Admits


A
Percent of samplein each decile
20
15
10
5
0
Whites
Blacks
Low
High
Terminal ICU use
B
Decedents using intensive care
100%
80%
60%
40%
20%
0%
Whites
Blacks
Low
High
Terminal ICU use

Don't….

- Include hospital-level characteristics (e.g., hospital fixed effects) in a patient-level regression.
  - *If 2 patients who differed only in race (1 black and 1 white, but otherwise with the same measured clinical characteristics) went to 2 different hospitals with the same measured characteristics (eg, teaching status, size), would they experience the same care and outcomes?*
    - Including hospital level characteristics in patient-level regressions can incorrectly attribute sources of variance between correlated variables such as a hospital and race

Do….

- Use multilevel (hierarchical) modeling, or
- Use individual hospital fixed effects (e.g., hospital ID) in patient-level regressions
  - *if a black and white patient with similar measured clinical characteristics went to the same hospital, would they experience the same care and outcomes different?*