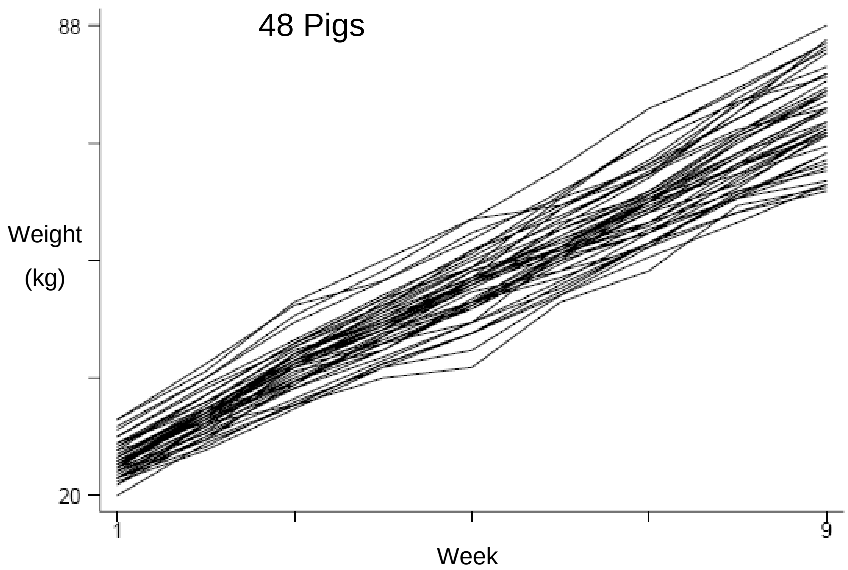
Lecture 3
Linear random intercept models

Example: Weight of Guinea Pigs

- Body weights of 48 pigs in 9 successive weeks of follow-up (Table 3.1 DLZ)
- The response is measures at n different times, or under n different conditions. In the guinea pigs example the time of measurement is referred to as a "within-units" factor. For the pigs n=9
- Although the pigs example considers a single treatment factor, it is straightforward to extend the situation to one where the groups are formed as the results of a factorial design (for example, if the pigs were separated into males and female and then allocated to the diet groups)

Pig Data



Pigs data model 1 – OLS fit

```
. regress weight time

      Source |       SS       df       MS              Number of obs =     432
-------------+------------------------------           F(  1,   430) = 5757.41
       Model |  111060.882     1  111060.882           Prob > F      =  0.0000
    Residual |  8294.72677   430  19.2900622           R-squared     =  0.9305
-------------+------------------------------           Adj R-squared =  0.9303
       Total |  119355.609   431  276.927167           Root MSE      =   4.392

------------------------------------------------------------------------------
      weight |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        time |   6.209896   .0818409    75.88   0.000     6.049038    6.370754
       _cons |   19.35561   .4605447    42.03   0.000     18.45041    20.26081
------------------------------------------------------------------------------
```

OLS results

Example: Weight of Pigs

For this type of repeated measures study we recognize two sources of random variation

1. Between: There is heterogeneity between pigs, due for example to natural biological (genetic?) variation
2. Within: There is random variation in the measurement process for a particular unit at any given time. For example, on any given day a particular guinea pig may yield different weight measurements due to differences in scale (equipment) and/or small fluctuations in weight during a day

A) Linear model with random intercept

$$Y_{ij} = U_i + \beta_0 + \beta_1 t_j + \varepsilon_{ij}$$

$$U_i \sim N(0, \tau^2)$$ Variance between

$$\varepsilon_{ij} \sim N(0, \sigma^2)$$ Variance within

$$\rho = \frac{\tau^2}{\tau^2 + \sigma^2}$$ Intraclass correlation coefficient! Why?

Intraclass correlation coefficient, i.e. correlation within measurements from pig i

$$\operatorname{corr}(Y_{ij}, Y_{ik}) = \frac{\operatorname{Cov}(Y_{ij}, Y_{ik})}{\sqrt{\operatorname{Var}(Y_{ij})}\sqrt{\operatorname{Var}(Y_{ij})}}$$

$$\operatorname{corr}(Y_{ij}, Y_{ik}) = \frac{\tau^2}{\sqrt{\tau^2 + \sigma^2}\sqrt{\tau^2 + \sigma^2}}$$

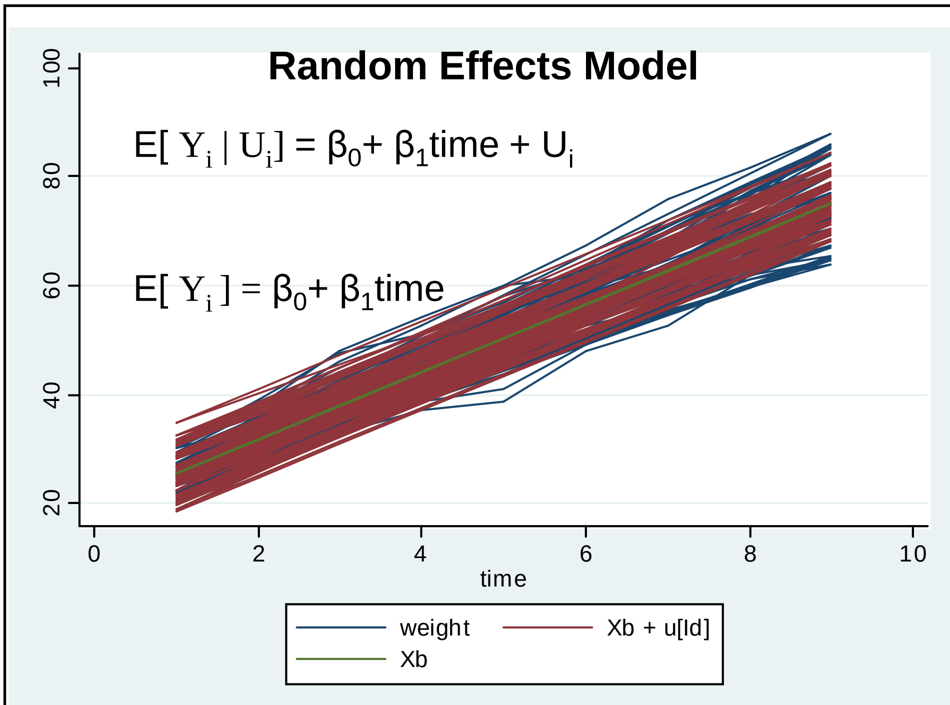
Pigs – RE model

```
xtreg weight time, re i(Id) mle

Random-effects ML regression                    Number of obs      =       432
Group variable (i): Id                          Number of groups   =        48

Random effects u_i ~ Gaussian                   Obs per group: min =         9
                                                               avg =       9.0
                                                               max =         9

                                                LR chi2(1)         =   1624.57
Log likelihood  = -1014.9268                    Prob > chi2        =    0.0000

------------------------------------------------------------------------------
      weight |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        time |   6.209896   .0390124   159.18   0.000     6.133433    6.286359
       _cons |   19.35561   .5974055    32.40   0.000     18.18472    20.52651
-------------+----------------------------------------------------------------
    /sigma_u |    3.84935   .4058114                      3.130767    4.732863
    /sigma_e |   2.093625   .0755471                       1.95067    2.247056
         rho |    .771714   .0393959                      .6876303    .8413114
------------------------------------------------------------------------------
```

Linear model with a random intercept - "conditional model"

Interpretation of results:

- Time effect: Among pigs with similar genetic variation (random effect), weight increases by 6.2 kg per week (95% CI: 6.1 to 6.3)
- Estimate of heterogeneity across pigs: sigma_u^2 = 3.8^2 = 14.4
- Estimate of variation in weights within a pig over time: sigma_e^2 = 2.1^2 = 4.4
- Fraction of total variability attributable to heterogeneity across pigs: 0.77
- This is also a measure of intraclass correlation, within pig correlation….



B) Marginal Model
With a Uniform or Exchangeable correlation structure

$$E[Y_{ij}] = \beta_0 + \beta_1 t_j$$ Model for the mean

$$\text{corr}(Y_{ij}, Y_{ik}) = \rho$$

$$\text{Var}(Y_{ij}) = \sigma_*^2 = (\tau^2 + \sigma^2)$$

$$\text{Cov}(Y_{ij}, Y_{ik}) = \rho(\tau^2 + \sigma^2)$$

Model for the covariance matrix

Pigs – Marginal model

```
xtreg weight time, pa i(Id) corr(exch)

Iteration 1: tolerance = 5.585e-15

GEE population-averaged model                   Number of obs      =       432
Group variable:                         Id      Number of groups   =        48
Link:                             identity      Obs per group: min =         9
Family:                           Gaussian                     avg =       9.0
Correlation:                  exchangeable                     max =         9
                                                Wald chi2(1)       =  25337.48
Scale parameter:                  19.20076      Prob > chi2        =    0.0000

------------------------------------------------------------------------------
      weight |      Coef.   Std. Err.       z     P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        time |   6.209896   .0390124   159.18    0.000     6.133433    6.286359
       _cons |   19.35561   .5974055    32.40    0.000     18.18472    20.52651
------------------------------------------------------------------------------
```

"Population Average", Marginal Model with Exchangeable Correlation structure results

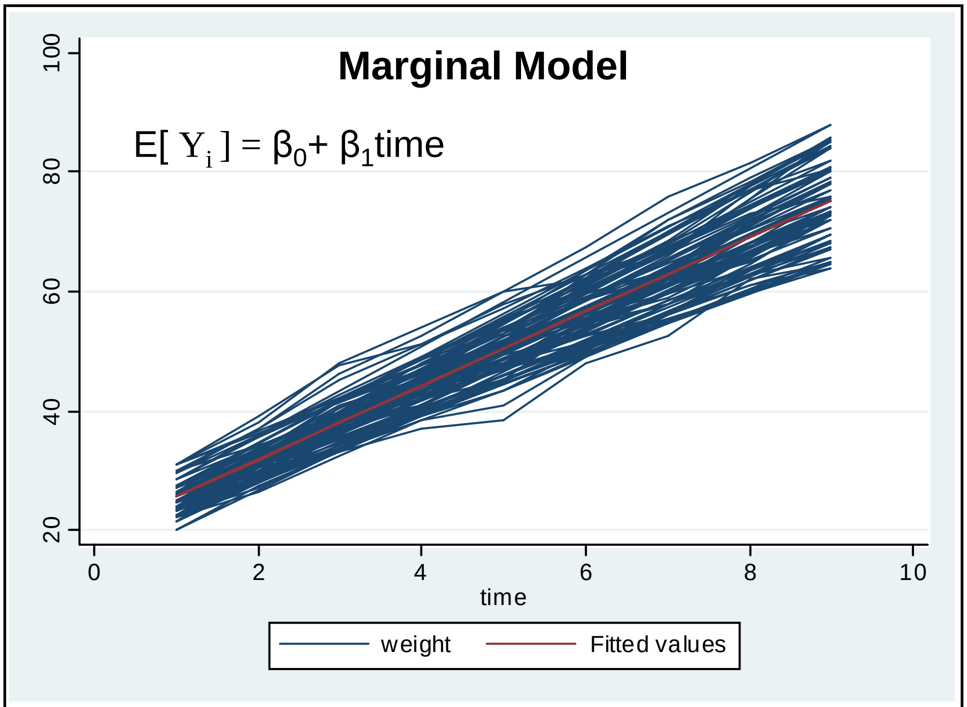
Pigs data model 1 – GEE fit

```
. xtgee weight time, i(Id) corr(exch)
. xtcorr
```

Estimated within-Id correlation matrix R:

	c1	c2	c3	c4	c5	c6	c7	c8	c9
r1	1.0000								
r2	0.7717	1.0000							
r3	0.7717	0.7717	1.0000						
r4	0.7717	0.7717	0.7717	1.0000					
r5	0.7717	0.7717	0.7717	0.7717	1.0000				
r6	0.7717	0.7717	0.7717	0.7717	0.7717	1.0000			
r7	0.7717	0.7717	0.7717	0.7717	0.7717	0.7717	1.0000		
r8	0.7717	0.7717	0.7717	0.7717	0.7717	0.7717	0.7717	1.0000	
r9	0.7717	0.7717	0.7717	0.7717	0.7717	0.7717	0.7717	0.7717	1.0000

GEE fit – Marginal Model with
Exchangeable Correlation structure results



Models A and B are equivalent

$$E[Y_{ij} \mid U_i] = U_i + \beta_0 + \beta_1 t_j$$

$$E[Y_{ij}] = E[E[Y_{ij} \mid U_i]] = \beta_0 + \beta_1 t_j$$

$$\text{cov}(Y_{ij}) = \text{cov}[E[Y_{ij} \mid U_i]] + E[\text{cov}[Y_{ij} \mid U_i]]$$

$$\text{cov}[E[Y_{ij} \mid U_i]] = \text{cov}(1U_i) = \tau^2 11'$$

$$E[\text{cov}[Y_{ij} \mid U_i]] = E[\sigma^2 I] = \sigma^2 I$$

$$\text{cov}(Y_{ij}) = (\tau^2 + \sigma^2)[\rho 11' + (1-\rho)I]$$

$$\rho = \frac{\tau^2}{\tau^2 + \sigma^2}$$

One group polynomial growth curve model

- Similarly, if you want to fit a quadratic curve
  $E[Y_{ij} \mid U_i] = U_i + \beta_0 + \beta_1 t_j + \beta_2 t_j^2$

$$E(\boldsymbol{Y}_i) = \begin{pmatrix} 1 & t_1 & t_1^2 \\ 1 & t_2 & t_2^2 \\ & \cdots & \\ 1 & t_n & t_n^2 \end{pmatrix} \begin{pmatrix} \beta_0 \\ \beta_1 \\ \beta_2 \end{pmatrix}$$

Pigs – Marg. model, quadratic trend

```
. xtgee weight time timesq, i(Id) corr(exch)

GEE population-averaged model                   Number of obs      =       432
Group variable:                         Id      Number of groups   =        48
Link:                             identity      Obs per group: min =         9
Family:                           Gaussian                     avg =       9.0
Correlation:                  exchangeable                     max =         9
                                                Wald chi2(2)       =  25387.68
Scale parameter:                  19.19317      Prob > chi2        =    0.0000

------------------------------------------------------------------------------
      weight |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        time |   6.358818   .1763801    36.05   0.000     6.013119    6.704517
      timesq |  -.0148922    .017202    -0.87   0.387    -.0486076    .0188231
       _cons |   19.08259   .6754833    28.25   0.000     17.75867    20.40651
------------------------------------------------------------------------------
```

Exchangeable Correlation structure results

Pigs data model 1 – GEE fit

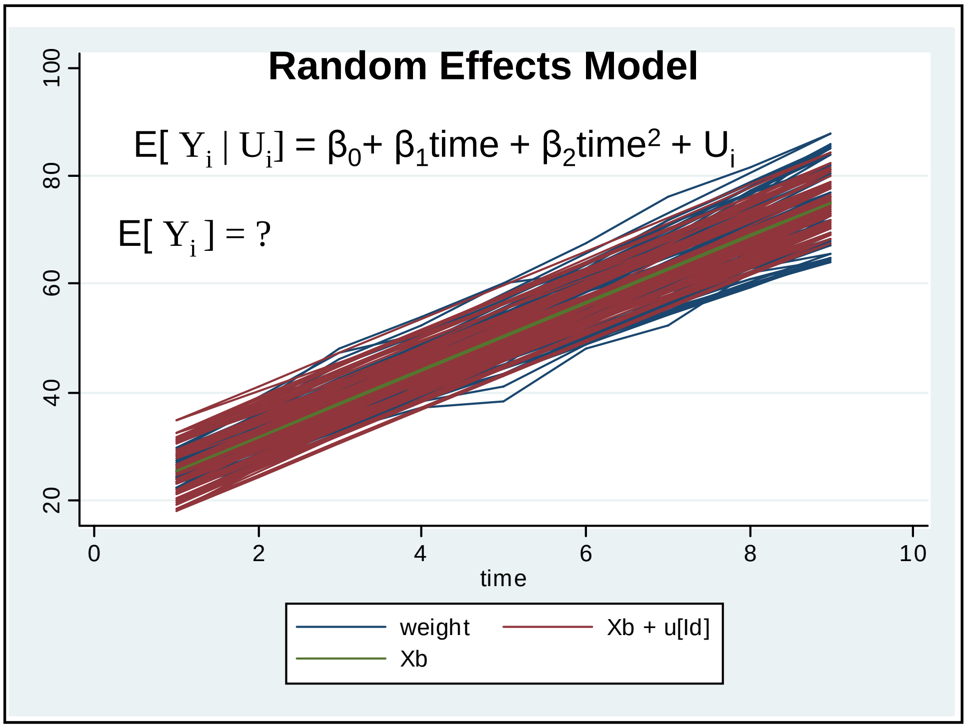
```
. xtcorr

Estimated within-Id correlation matrix R:

        c1      c2      c3      c4      c5      c6      c7      c8      c9
r1  1.0000
r2  0.7721  1.0000
r3  0.7721  0.7721  1.0000
r4  0.7721  0.7721  0.7721  1.0000
r5  0.7721  0.7721  0.7721  0.7721  1.0000
r6  0.7721  0.7721  0.7721  0.7721  0.7721  1.0000
r7  0.7721  0.7721  0.7721  0.7721  0.7721  0.7721  1.0000
r8  0.7721  0.7721  0.7721  0.7721  0.7721  0.7721  0.7721  1.0000
r9  0.7721  0.7721  0.7721  0.7721  0.7721  0.7721  0.7721  0.7721  1.0000
```

GEE fit – Marginal Model with
Exchangeable Correlation structure results

Pigs – RE model, quadratic trend

```
. gen timesq = time*time
. xtreg weight time timesq, re i(Id) mle

Random-effects ML regression                    Number of obs      =       432
Group variable (i): Id                          Number of groups   =        48

Random effects u_i ~ Gaussian                   Obs per group: min =         9
                                                               avg =       9.0
                                                               max =         9

                                                LR chi2(2)         =   1625.32
Log likelihood  = -1014.5524                    Prob > chi2        =    0.0000

------------------------------------------------------------------------------
      weight |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        time |   6.358818   .1763799    36.05   0.000      6.01312    6.704516
      timesq |  -.0148922    .017202    -0.87   0.387    -.0486075    .0188231
       _cons |   19.08259    .675483    28.25   0.000     17.75867    20.40651
-------------+----------------------------------------------------------------
    /sigma_u |   3.849473   .4057983                      3.130909    4.732951
    /sigma_e |   2.091585   .0754733                      1.948769    2.244866
         rho |   .7720686   .0393503                      .6880712    .8415775
------------------------------------------------------------------------------
```

Exchangeable Correlation structure results



Pigs – Marginal model: AR(1)

```
xtgee weight time, i(Id) corr(AR1) t(time)

GEE population-averaged model                   Number of obs      =       432
Group and time vars:                 Id time    Number of groups   =        48
Link:                               identity    Obs per group: min =         9
Family:                             Gaussian                   avg =       9.0
Correlation:                           AR(1)                   max =         9
                                                Wald chi2(1)       =   6254.91
Scale parameter:                    19.26754    Prob > chi2        =    0.0000

------------------------------------------------------------------------------
      weight |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        time |   6.272089   .0793052    79.09   0.000     6.116654    6.427524
       _cons |   18.84218   .6745715    27.93   0.000     17.52004    20.16431
------------------------------------------------------------------------------
```

GEE-fit Marginal Model with AR1 Correlation structure

Pigs – RE model: AR(1)

```
xtregar weight time

RE GLS regression with AR(1) disturbances       Number of obs      =       432
Group variable (i): Id                          Number of groups   =        48

R-sq:  within  = 0.9851                         Obs per group: min =         9
       between = 0.0000                                        avg =       9.0
       overall = 0.9305                                        max =         9

                                                Wald chi2(2)       =  12688.55
corr(u_i, Xb)       = 0 (assumed)               Prob > chi2        =    0.0000

------------------------------------------------------------------------------
      weight |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        time |   6.257651   .0555527   112.64   0.000      6.14877    6.366533
       _cons |   19.00945   .6281622    30.26   0.000     17.77827    20.24062
-------------+----------------------------------------------------------------
      rho_ar |  .73091237   (estimated autocorrelation coefficient)
     sigma_u |   3.583343
     sigma_e |  1.5590851
     rho_fov |  .84082696   (fraction of variance due to u_i)
       theta |  .60838037
------------------------------------------------------------------------------
```

Random effects model with AR1 Correlation structure

Important Points

- Modeling the correlation in longitudinal data is important to be able to obtain correct inferences on regression coefficients β
- There are correspondences between random effect and marginal models in the linear case because the interpretation of the regression coefficients is the same as that in standard linear regression