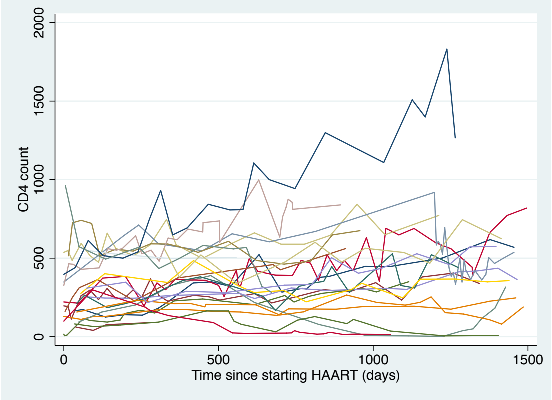

Longitudinal Data
Fall 2015

Chapter 7, Part II

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

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Hierarchical Models
pH vs. CO2

- Functional opthalmologic study of the impact of CO_2 levels on pH in eyes (Cohen, et al., 1992).

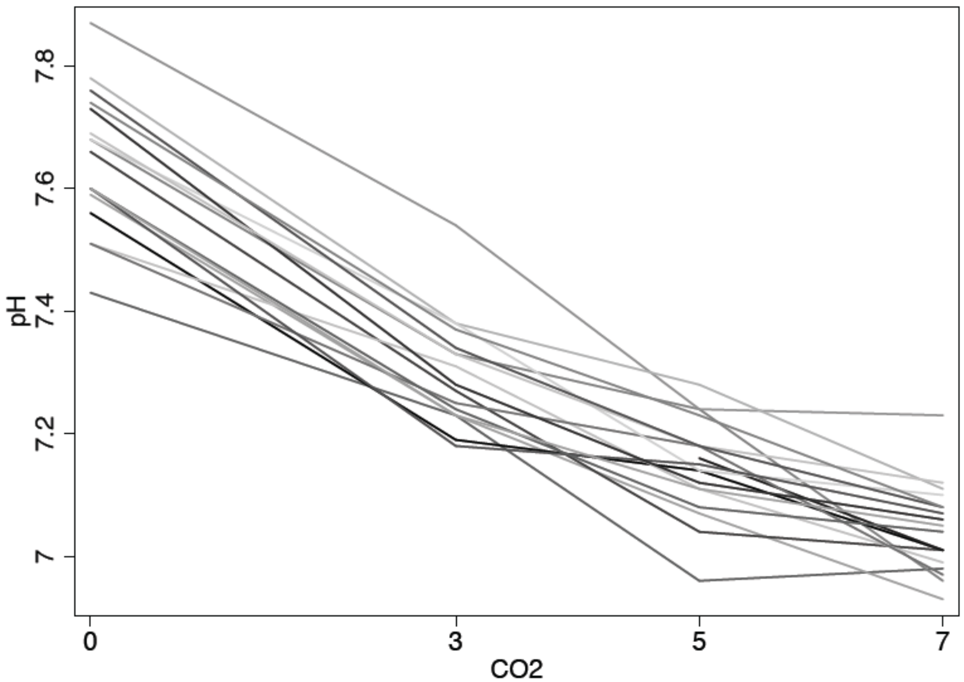
- 18 subjects, at two different visits, were fit with specialized goggles that regulated exposure to CO2 (different levels for each eye) and subsequent measures were made of pH.

- Thus, the data consist of 18x4=72 nested measurements of eyes within visits within subjects.

- The outcome, pH, to be Y_{ijk}, for the ith person, jth visit, kth eye: $i=(1,\ldots,m=18), j=(1,2), k=(1,2)$.

Data

	id	co2	ph	prph	visit	eye
1	1	0	7.432	76.4	1	1
2	1	5	6.956	59.4	1	2
3	1	3	7.232	80.3	2	1
4	1	7	6.982	74.2	2	2
5	2	0	7.594	67.8	1	1
6	2	7	6.929	61.1	1	2
7	2	3	7.230	73.4	2	1
8	2	5	7.073	65.9	2	2
9	3	3	7.329	87.6	1	1
10	3	7	6.963	55.8	1	2



Fitting the following Sequence of Models

- Model 1

$$Y_{ijk} = \beta_0 + \beta_1 X_{ijk} + \beta_2 (X_{ijk})^2 + e_{ijk}$$

- Model 2

$$Y_{ijk} = \beta_0 + \beta_{0i} + \beta_1 X_{ijk} + \beta_2 (X_{ijk})^2 + e_{ijk}$$

- Model 3

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

- Model 4

$$Y_{ijk} = \beta_0 + \beta_{0i} + (\beta_1 + \beta_{1i}) X_{ijk} + \beta_2 (X_{ijk})^2 + e_{ijk}$$

Model 1

$$Y_{ijk} = \beta_0 + \beta_1 X_{ijk} + \beta_2 (X_{ijk})^2 + e_{ijk}$$

- $E(e_{ijk})=0$, $cov(e_{ijk}, e_{ij'k'})=0$, $j \neq j'$ or $k \neq k$.

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

- What does V_0 look like for this model?

- How does one interpret the parameters, β_0, β_1, and β_2?

Model 1

```
.mixed ph co2 co22, stddev reml

Mixed-effects REML regression                   Number of obs      =        70

                                                Wald chi2(2)       =    463.58
Log restricted-likelihood =  58.499944          Prob > chi2        =    0.0000

------------------------------------------------------------------------------
          ph |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         co2 |  -.1373144   .0137997    -9.95   0.000    -.1643613   -.1102674
        co22 |   .0073496   .0019106     3.85   0.000     .0036049    .0110942
       _cons |   7.646126   .0212018   360.64   0.000     7.604572    7.687681
------------------------------------------------------------------------------
------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
               sd(Residual) |   .0883141   .0074639      .0748325    .1042245
------------------------------------------------------------------------------

estat ic
-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
      model1 |     70          .    58.49994      4    -108.9999   -100.0059
-----------------------------------------------------------------------------
```

Getting Measures of Association

```
. lincom 3*co2+9*co22    E(Y|CO2=3)-E(Y|CO2=0)

 ( 1)  3*[ph]co2 + 9*[ph]co22 = 0

------------------------------------------------------------------------------
          ph |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         (1) |  -.3457971   .0254904   -13.57   0.000    -.3957574   -.2958368
------------------------------------------------------------------------------


. lincom 5*co2+25*co22   E(Y|CO2=5)-E(Y|CO2=0)


  ( 1)  5*[ph]co2 + 25*[ph]co22 = 0

------------------------------------------------------------------------------
          ph |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         (1) |   -.502833   .0273284   -18.40   0.000    -.5563957   -.4492703
------------------------------------------------------------------------------

. lincom 7*co2+49*co22   E(Y|CO2=7)-E(Y|CO2=0)

 ( 1)  7*[ph]co2 + 49*[ph]co22 = 0

------------------------------------------------------------------------------
          ph |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         (1) |  -.6010725   .0286516   -20.98   0.000    -.6572287   -.5449163
------------------------------------------------------------------------------
```

Model 2

$$Y_{ijk} = \beta_0 + \beta_{0i} + \beta_1 X_{ijk} + \beta_2 (X_{ijk})^2 + e_{ijk}$$

- How does one interpret the parameters, β_0, $\beta_{0i,}$ and β_1, β_2?
- $E(e_{ijk})=0$, $cov(e_{ijk}, e_{ij'k'})=0$, $j \neq j'$ or $k \neq k'$
- Var(e_{ijk})= $\sigma^2{}_e$
- $Var(\beta_{0i})$= $\sigma^2{}_{\beta 0i.}$
- cov($e_{ijk,}$ β_{0i})= 0.
- What does V_0 look like for this model?

Model 2

```
.mixed ph co2 co22 || id:, stddev reml
                                                  Wald chi2(2)       =   1346.68
Log restricted-likelihood =  76.647278           Prob > chi2        =    0.0000

------------------------------------------------------------------------------
          ph |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         co2 |  -.1372775   .0080292   -17.10   0.000    -.1530143   -.1215406
        co22 |   .0073546   .0011116     6.62   0.000     .0051759    .0095334
       _cons |    7.64567   .0209821   364.39   0.000     7.604546    7.686795
------------------------------------------------------------------------------

------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
                   sd(_cons) |   .0715285   .0138821      .0488968    .1046354
-----------------------------+------------------------------------------------
                sd(Residual) |   .0513741   .0051277      .0422459    .0624746
------------------------------------------------------------------------------
LR test vs. linear regression: chibar2(01) =    36.29 Prob >= chibar2 = 0.0000

Residual intraclass correlation

------------------------------------------------------------------------------
                       Level |        ICC   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
                          id |   .6596925   .1004796      .4463808    .8233416
------------------------------------------------------------------------------
-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
      model2 |     70           .    76.64728      5    -143.2946   -132.0521
-----------------------------------------------------------------------------
```

Model 3

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

- How does one interpret the parameters, β_0, β_{0i}, β_{0ij} and β_1, β_2?
- $E(e_{ijk})=0$, $cov(e_{ijk}, e_{ij'k'})=0$, $j \neq j'$ or $k \neq k'$
- $Var(e_{ijk}) = \sigma^2_e$
- $Var(\beta_{0i}) = \sigma^2_{id}$
- $Var(\beta_{0ij}) = \sigma^2_{visit}$
- $cov(e_{ijk}, \beta_{0i}) = 0$, $cov(e_{ijk}, \beta_{0ij}) = 0$, $cov(\beta_{0i}, \beta_{0ij}) = 0$
- What does V_0 look like for this model?

Model 3

```
mixed ph co2 co22 || id: || visit:, stddev

-----------------------------------------------------------
                |   No. of       Observations per Group
 Group Variable |   Groups    Minimum    Average    Maximum
----------------+------------------------------------------
             id |       18          2        3.9          4
          visit |       35          2        2.0          2
-----------------------------------------------------------

                                                Wald chi2(2)       =   1456.58
Log likelihood =  91.091123                     Prob > chi2        =    0.0000

------------------------------------------------------------------------------
          ph |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         co2 |  -.1364223   .0078051   -17.48   0.000    -.1517199   -.1211246
        co22 |   .0072612   .0010794     6.73   0.000     .0051455    .0093768
       _cons |   7.644394   .0203644   375.38   0.000     7.604481    7.684308
------------------------------------------------------------------------------


------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
                   sd(_cons) |   .0684105   .0134426      .0465439    .1005501
-----------------------------+------------------------------------------------
visit: Identity              |
                   sd(_cons) |   .0208853   .0144296       .005392    .0808969
-----------------------------+------------------------------------------------
                sd(Residual) |   .0474441    .005692      .0375026    .0600211
------------------------------------------------------------------------------
LR test vs. linear regression:       chi2(2) =    38.01   Prob > chi2 = 0.0000
```

Model 3

```
estat icc

Residual intraclass correlation

------------------------------------------------------------------------------
                       Level |        ICC   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
                          id |   .6352526   .1100754       .407022    .8154659
                    visit|id |   .6944611   .0985583      .4776825    .8495975
------------------------------------------------------------------------------

. estat ic

-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
           . |     70           .    91.09112      6    -170.1822   -156.6913
-----------------------------------------------------------------------------
```

Model 4

$$Y_{ijk} = \beta_0 + \beta_{0i} + (\beta_1 + \beta_{1i})X_{ijk} + \beta_2 (X_{ijk})^2 + e_{ijk}$$

- $E(e_{ijk})=0$, $cov(e_{ijk}, e_{ij'k'})=0$, $j \neq j'$ or $k \neq k'$
- $Var(e_{ijk}) = \sigma^2_e$
- $Var(\beta_{0i}) = \sigma^2_0$, $Var(\beta_{1i}) = \sigma^2_1$
- $cov(e_{ijk}, \beta_{0i}) = 0$, $cov(e_{ijk}, \beta_{1i}) = 0$, $cov(\beta_{0i}, \beta_{1i}) = \sigma_{01}$.
- What does variance-covariance of random effects look like?
- How does one interpret the parameters, β_0, β_{0i}, β_{1i}, and β_1, β_2?

Model 4

```
.mixed ph co2 co22 || id: co2, covariance(un)


                                                Wald chi2(2)      =    1109.29
Log likelihood =   94.57083                     Prob > chi2       =     0.0000

------------------------------------------------------------------------------
          ph |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         co2 |  -.1372451   .0074464   -18.43   0.000    -.1518399   -.1226504
        co22 |   .0073501   .0010082     7.29   0.000      .005374    .0093262
       _cons |   7.645654   .0249892   305.96   0.000     7.596676    7.694632
------------------------------------------------------------------------------


------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Unstructured             |
                    var(co2) |   .0000404   .0000312      8.88e-06    .0001837
                  var(_cons) |   .0088415   .0035064       .004064    .0192352
              cov(co2,_cons) |  -.0005976   .0003306     -.0012456    .0000504
-----------------------------+------------------------------------------------
               var(Residual) |    .002172   .0004247      .0014805    .0031864
------------------------------------------------------------------------------
LR test vs. linear regression:       chi2(3) =    44.97   Prob > chi2 = 0.0000
```

Model 4

```
. estat icc

Conditional intraclass correlation

------------------------------------------------------------------------------
                       Level |        ICC   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
                          id |   .8027868   .0711758      .6277709    .9076223
------------------------------------------------------------------------------


 . estat ic

Akaike's information criterion and Bayesian information criterion

-----------------------------------------------------------------------------
       Model |    Obs    ll(null)   ll(model)     df          AIC         BIC
-------------+---------------------------------------------------------------
           . |     70           .    94.57083      7    -175.1417   -159.4022
-----------------------------------------------------------------------------
```

Comparing Models

Table 7.4: ESTIMATES(SE) AND AKAIKE'S INFORMATION CRITERION (AIC) OF FOUR HIERARCHICAL LINEAR MIXED EFFECTS MODELS FOR PH VERSUS $C0_2$

	Model 1		Model 2		Model 3		Model 4	
Parameter	Est	SE	Est	SE	Est	SE	Est	SE
β_0	7.6	.021	7.6	.021	7.6	.020	7.6	.025
β_1	-.14	.014	-.14	.008	-.14	.0078	-.14	.0074
β_2	.0073	.0019	.0074	.0011	.0073	.0011	.0074	.0010
$E(Y_{ijk} \mid X_{ijk} = 5) - E(Y_{ijk} \mid X_{ijk} = 0)$	-.50	.027	-.50	.016	-.50	.015	-.50	.016
$\sigma_{\beta_{0i}}$			.072	.014	.068	.014	.094	.019
$\sigma_{\beta_{0ij}}$					.021	.013		
$\sigma_{\beta_{1i}}$							.0064	.0025
σ_e	.088	.0075	.051	.0051	.047	.0057	.047	.0046
AIC	-109		-143		-170		-175	

Model 4, Robust

```
.mixed ph co2 co22 || id: co2, covariance(un) stddev ro


                                                Wald chi2(2)      =    1260.49
Log pseudolikelihood =   94.57083               Prob > chi2       =     0.0000

                                    (Std. Err. adjusted for 18 clusters in id)
------------------------------------------------------------------------------
             |               Robust
          ph |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
         co2 |  -.1372451   .0080234   -17.11   0.000    -.1529707   -.1215196
        co22 |   .0073501     .00105     7.00   0.000     .0052922    .0094081
       _cons |   7.645654   .0263427   290.24   0.000     7.594023    7.697285
------------------------------------------------------------------------------

------------------------------------------------------------------------------
                             |               Robust
  Random-effects Parameters  |   Estimate   Std. Err.     [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Unstructured             |
                     sd(co2) |   .0063553   .0014507       .004063     .009941
                   sd(_cons) |   .0940291   .0169891      .0659884    .1339852
             corr(co2,_cons) |         -1   7.38e-09            -1   -.9999999
-----------------------------+------------------------------------------------
                sd(Residual) |   .0466047   .0038592      .0396228    .0548169
------------------------------------------------------------------------------
```

Naïve vs Robust

Table 7.5: COMPARISONS OF NAIVE AND ROBUST INFERENCE FOR MODEL 4

	Est	SE Naive	SE Robust
β_0	7.6	.025	.026
β_1	-.14	.0074	.0080
β_2	.0074	.0010	.0010
$E(Y_{ijk} \mid X_{ijk} = 5) - E(Y_{ijk} \mid X_{ijk} = 0)$	-.50	.016	.017
$\sigma_{\beta_{0i}}$	.094	.019	.017
$\sigma_{\beta_{1i}}$	.0064	.0025	.0014
σ_e	.047	.0046	.0039