Example Analysis with STATA

- Exploratory Data Analysis
  - Means and Variance by Time and Group
  - Correlation
  - Individual Series
- Derived Variable Analysis
  - Fitting a Line to Each Subject
  - Summarizing Slopes by Group
- Regression Analysis
  - Using Linear Mixed Model (`xtmixed; gllamm`)
  - Using GEE

CF Data – Summary

- Cystic Fibrosis Data
  - **Subjects**: A total of N=200 subjects enrolled in a cohort study (patient registry).
  - **Observation-level Measures**:
    - `FEV1` – measure of pulmonary function
    - `AGE` – age in years
  - **Person-level Measures**:
    - `GENDER` – male / female
    - `F508` – genotype (number of alleles)
    - `AGE0` – age-at-entry to study
- **Q**: Is level and/or rate of decline in pulmonary function associated with gender and/or genotype?

Example: CF Data

```
*************************************************************
* cfkids.do                                                 *
*************************************************************
*                                                           *
* PURPOSE:  analysis of FEV1 among CF kids                  *
*                                                           *
* AUTHOR:  P. Heagerty                                      *
*                                                           *
* DATE:  31 March 2005                                      *
*        04 March 2006                                      *
*************************************************************

infile id fev1 age gender pseudoA f508 pancreat using NewCFkids.raw

*
```

```
*  ID       = patient id
*  FEV1     = percent-predicted forced expiratory volume in 1 second
*  AGE      = age (years)
*  GENDER   = sex (1=male, 2=female)
*  PSEUDOA  = infection with Pseudo Aeruginosa (0=no, 3=yes)
*  F508     = genotype (1=homozygous, 2=heterozygous, 3=none)
*  PANCREAT = pancreatic enzyme supplmentation (0,1=no, 2=yes)
*

label variable age "Age (years)"

recode gender 1=0 2=1
label variable gender "female"

recode pseudoA 3=1

recode pancreat 1=0 2=1
```

```
recode f508 1=2 2=1 3=0

save NewCFkids, replace

***
*** some exploratory data analysis -- observation level
***

summarize  fev1

gen y8 = fev1
recode y8 (min/max=.) if age > 8.75
recode y8 (min/max=.) if age < 7.25

gen y10 = fev1
recode y10 (min/max=.) if age > 10.75
recode y10 (min/max=.) if age < 9.25
```

```
gen y12 = fev1
recode y12 (min/max=.) if age > 12.75
recode y12 (min/max=.) if age < 11.25

gen y14 = fev1
recode y14 (min/max=.) if age > 14.75
recode y14 (min/max=.) if age < 13.25

gen y16 = fev1
recode y16 (min/max=.) if age > 16.75
recode y16 (min/max=.) if age < 15.25

gen y18 = fev1
recode y18 (min/max=.) if age > 18.75
recode y18 (min/max=.) if age < 17.25

gen y20 = fev1
recode y20 (min/max=.) if age > 20.75
```

```
recode y20 (min/max=.) if age < 19.25

***** the following creates a single record per kid:

collapse (mean) f508 gender y8 y10 y12 y14 y16 y18 y20, by(id)


***** look at means over these ages:

summarize

sort f508
by f508: summarize

sort gender
by gender: summarize
```

Results: CF Data

```
. summarize  fev1
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
        fev1 |      1513    70.36416    27.22294       11.03     159.67
```

Results: CF Data

```
. summarize
    Variable |        Obs        Mean    Std. Dev.       Min        Max
-------------+---------------------------------------------------------
          id |        200    109141.9    5701.099    100073     119028
        f508 |        200       1.335    .6745741         0          2
      gender |        200         .49    .5011544         0          1
-------------+---------------------------------------------------------
          y8 |         63    84.18426    25.81721     24.33      136.5
         y10 |         81    80.96802    24.22817    24.645     119.95
         y12 |        104    76.45958    26.55931     17.36     136.97
         y14 |        116     72.9857     25.0613      14.2    134.415
         y16 |        103    68.17985    26.34962     18.05     148.22
         y18 |         90    66.46433    25.04077     21.25     136.51
         y20 |         78    61.86303    25.19371     14.63     118.04
```

Results: CF Data

-> f508 = 0

Variable	Obs	Mean	Std. Dev.	Min	Max
f508	23	0	0	0	0
y8	7	77.16214	24.50721	42.29	108.135
y10	8	73.28375	31.3521	24.645	108
y12	9	73.58333	34.82344	17.36	136.97
y14	12	82.67667	18.84188	43.51	104.88
y16	14	77.37286	25.45999	34.87	115.63
y18	11	86.28864	23.54095	42.97	109.78
y20	10	81.47	27.00938	26.93	118.04

Results: CF Data

-> f508 = 1

Variable	Obs	Mean	Std. Dev.	Min	Max
f508	87	1	0	1	1
y8	25	83.4214	25.86229	39.845	117.7
y10	29	83.15086	22.07282	27.69	118.14
y12	38	77.83184	23.68194	24.26	123.39
y14	42	71.37131	25.35112	22.88	134.415
y16	38	67.60211	25.62312	21.39	148.22
y18	38	61.38513	21.67322	27.22	114.78
y20	34	61.33976	24.50993	21.65	110.29

Results: CF Data

```
-> f508 = 2
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
        f508 |        90           2           0         2          2
-------------+--------------------------------------------------------
          y8 |        31    86.38511    26.55727     24.33      136.5
         y10 |        44    80.92648    24.50779        31     119.95
         y12 |        57    75.99889    27.40096     23.45     123.47
         y14 |        62    72.20366    25.82999      14.2      126.1
         y16 |        51    66.08676     27.0853     18.05    125.655
         y18 |        41    65.85317    26.25174     21.25     136.51
         y20 |        34    56.61956    23.15649     14.63     109.68
```

Results: CF Data

-> gender = 0

Variable	Obs	Mean	Std. Dev.	Min	Max
gender	102	0	0	0	0
y8	38	85.9443	23.94876	38.42	122.61
y10	44	84.60659	23.16013	24.645	119.95
y12	56	79.9042	25.34632	17.36	136.97
y14	60	74.02294	21.95634	27.8	134.415
y16	50	72.0945	24.3662	31.315	120.52
y18	42	67.6119	24.78879	26.09	112.74
y20	37	63.53477	28.72807	14.63	118.04

Results: CF Data

```
-> gender = 1
    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
      gender |        98           1           0         1          1
-------------+--------------------------------------------------------
          y8 |        25      81.509     28.7279     24.33      136.5
         y10 |        37    76.64108    25.06672     27.69     111.97
         y12 |        48    72.44087    27.63062     23.45     123.47
         y14 |        56    71.87437    28.17201      14.2      126.1
         y16 |        53    64.48679    27.81735     18.05     148.22
         y18 |        48    65.46021    25.47799     21.25     136.51
         y20 |        41    60.35439    21.77503     21.65     109.68
```

Example: CF Data

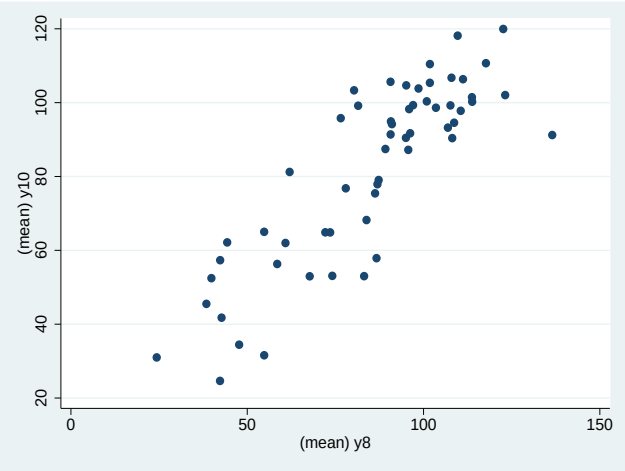
```
***** information on correlation

corr y8 y10 y12
corr y12 y14 y16
corr y16 y18 y20

graph twoway (scatter y14 y8)
graph twoway (scatter y12 y8)
graph twoway (scatter y10 y8)

graph twoway (scatter y16 y10)
graph twoway (scatter y14 y10)
graph twoway (scatter y12 y10)
```

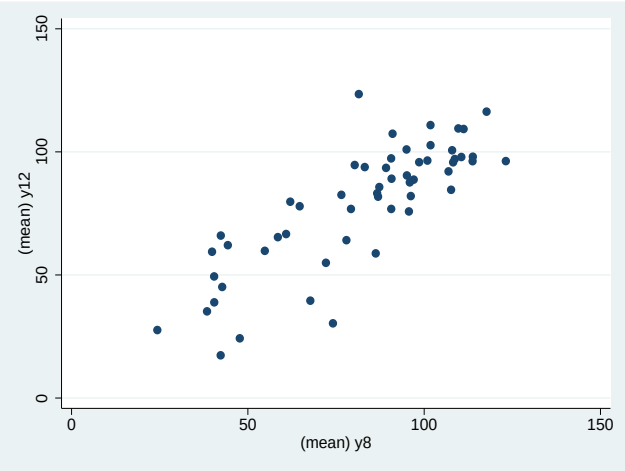
Results: CF Data

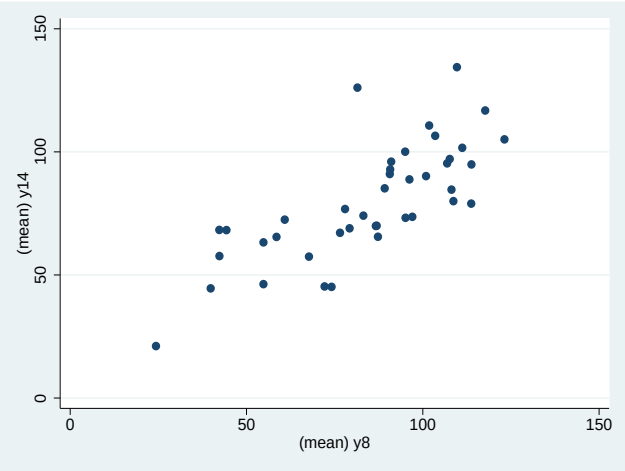
```
. corr y8 y10 y12
(obs=50)
             |       y8      y10      y12
-------------+---------------------------
          y8 |   1.0000
         y10 |   0.8682   1.0000
         y12 |   0.8032   0.8904   1.0000

. corr y12 y14 y16
(obs=53)
             |      y12      y14      y16
-------------+---------------------------
         y12 |   1.0000
         y14 |   0.7904   1.0000
         y16 |   0.6918   0.8830   1.0000
```

```
. corr y16 y18 y20
(obs=47)
             |      y16      y18      y20
-------------+---------------------------
         y16 |   1.0000
         y18 |   0.8662   1.0000
         y20 |   0.8088   0.8638   1.0000
```

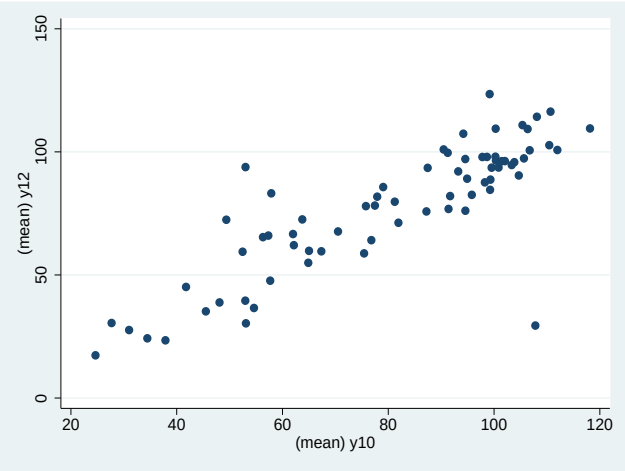
Results: CF Data – Pairwise Plots

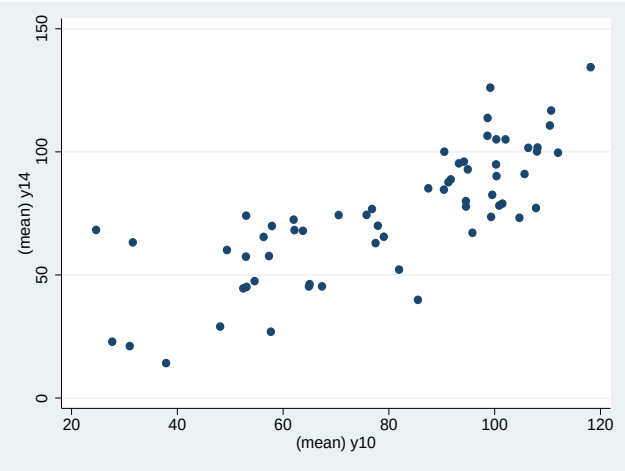


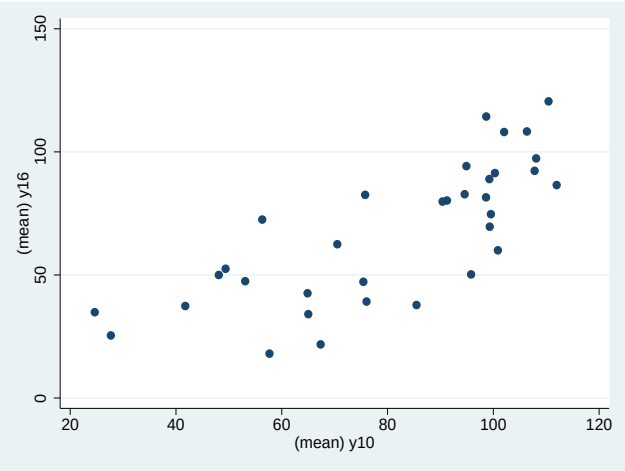




Results: CF Data – Pairwise Plots







Example: CF Data

```
***
*** some exploratory data analysis -- person level
***

clear

use NewCFkids

collapse (min) age f508 gender, by(id)

tab f508
tab gender
tab f508 gender
```

Results: CF Data

f508	Freq.	Percent	Cum.
0	23	11.50	11.50
1	87	43.50	55.00
2	90	45.00	100.00
Total	200	100.00	

gender	Freq.	Percent	Cum.
0	102	51.00	51.00
1	98	49.00	100.00
Total	200	100.00	

Results: CF Data

```
. tab f508 gender

           |     (min) gender
(min) f508 |         0          1 |     Total
-----------+----------------------+----------
         0 |        13         10 |        23
         1 |        46         41 |        87
         2 |        43         47 |        90
-----------+----------------------+----------
     Total |       102         98 |       200
```

Example: CF Data

```
***
*** add the age-at-entry to the data
***

gen age0 = age

drop age f508 gender

***** save data with just ID and age0
save NewCFage0, replace

***** return to original data, and merge
clear

use NewCFkids
```

```
sort id

merge id using NewCFage0

list in 1/4

***** create ageL and save
gen ageL = age - age0

save NewCFkids, replace
```

Results: CF Data

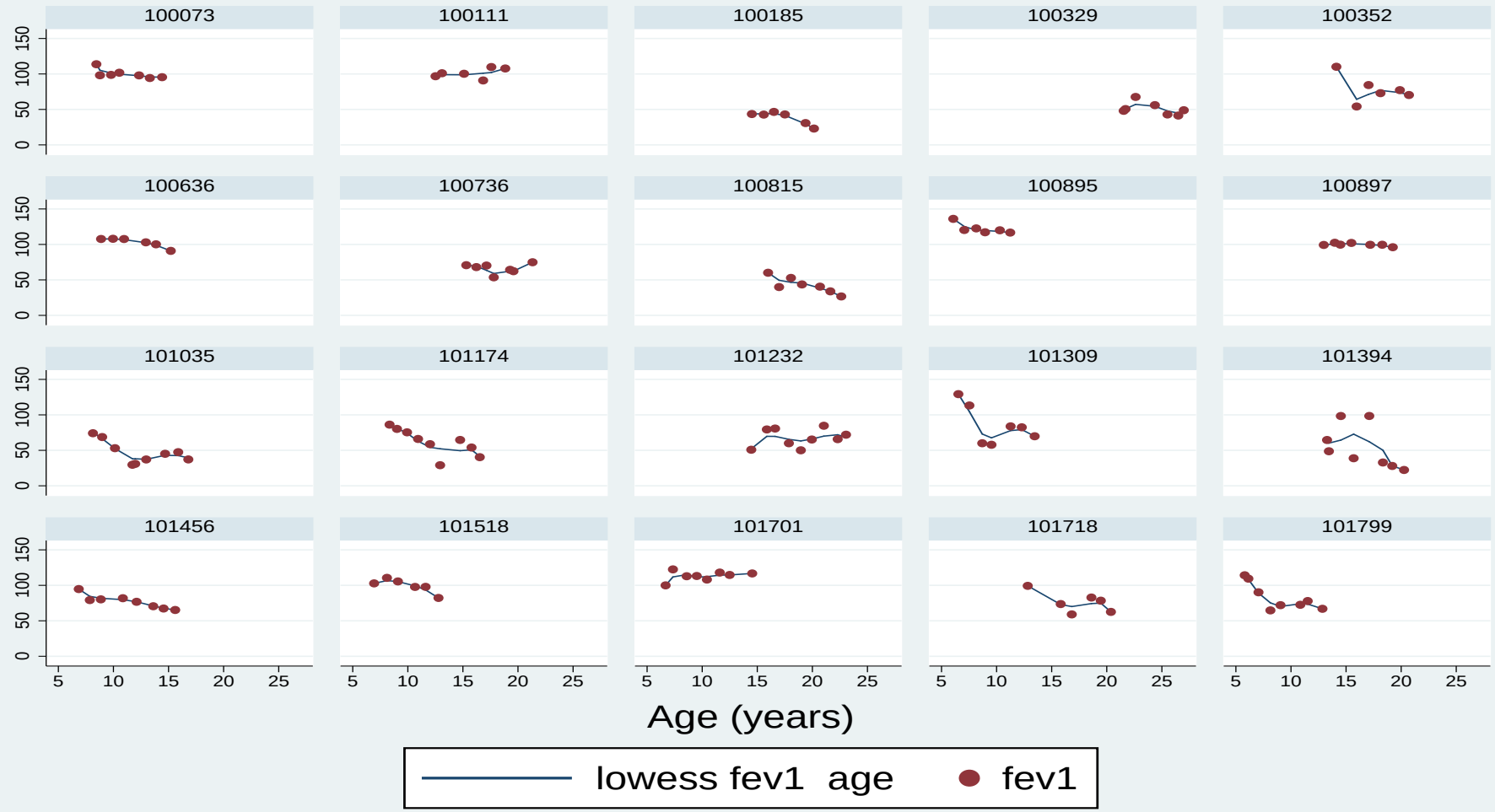
```
. list in 1/4
   +-----------------------------------------------------------------------+
1. |     id |   fev1 |    age | gender | pseudoA | f508 | pancreat |  age0 |
   | 100073 |  113.8 |  8.452 |      1 |       1 |    2 |        1 | 8.452 |
   |-----------------------------------------------------------------------|
2. |     id |   fev1 |    age | gender | pseudoA | f508 | pancreat |  age0 |
   | 100073 |  98.18 |  8.783 |      1 |       1 |    2 |        1 | 8.452 |
   |-----------------------------------------------------------------------|
3. |     id |   fev1 |    age | gender | pseudoA | f508 | pancreat |  age0 |
   | 100073 |  98.73 |  9.785 |      1 |       1 |    2 |        1 | 8.452 |
   |-----------------------------------------------------------------------|
4. |     id |   fev1 |    age | gender | pseudoA | f508 | pancreat |  age0 |
   | 100073 | 101.79 | 10.538 |      1 |       1 |    2 |        1 | 8.452 |
   +-----------------------------------------------------------------------+
```

Example: CF Data

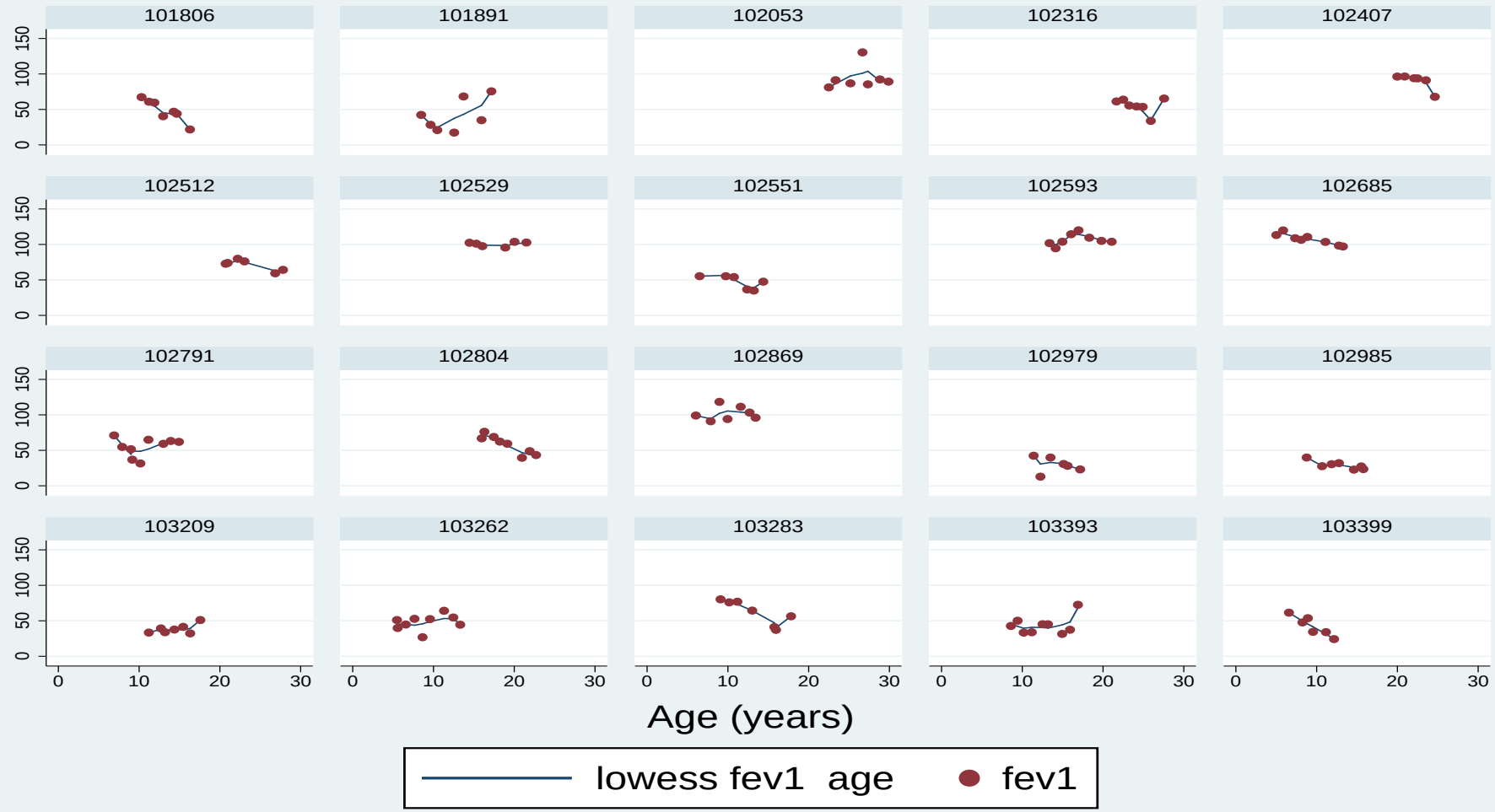
```
***
*** plot some individual series
***

graph twoway (lowess fev1 age) (scatter fev1 age) ///
      if (id<=101799), by(id)

graph twoway (lowess fev1 age) (scatter fev1 age) ///
      if (id>101799 & id<=103399), by(id)

***
*** plot some fitted lines
***

graph twoway (lfit fev1 age) (scatter fev1 age) ///
```

```
      if (id<=101799), by(id)

graph twoway (lfit fev1 age) (scatter fev1 age) ///
      if (id>101799 & id<=103399), by(id)
```

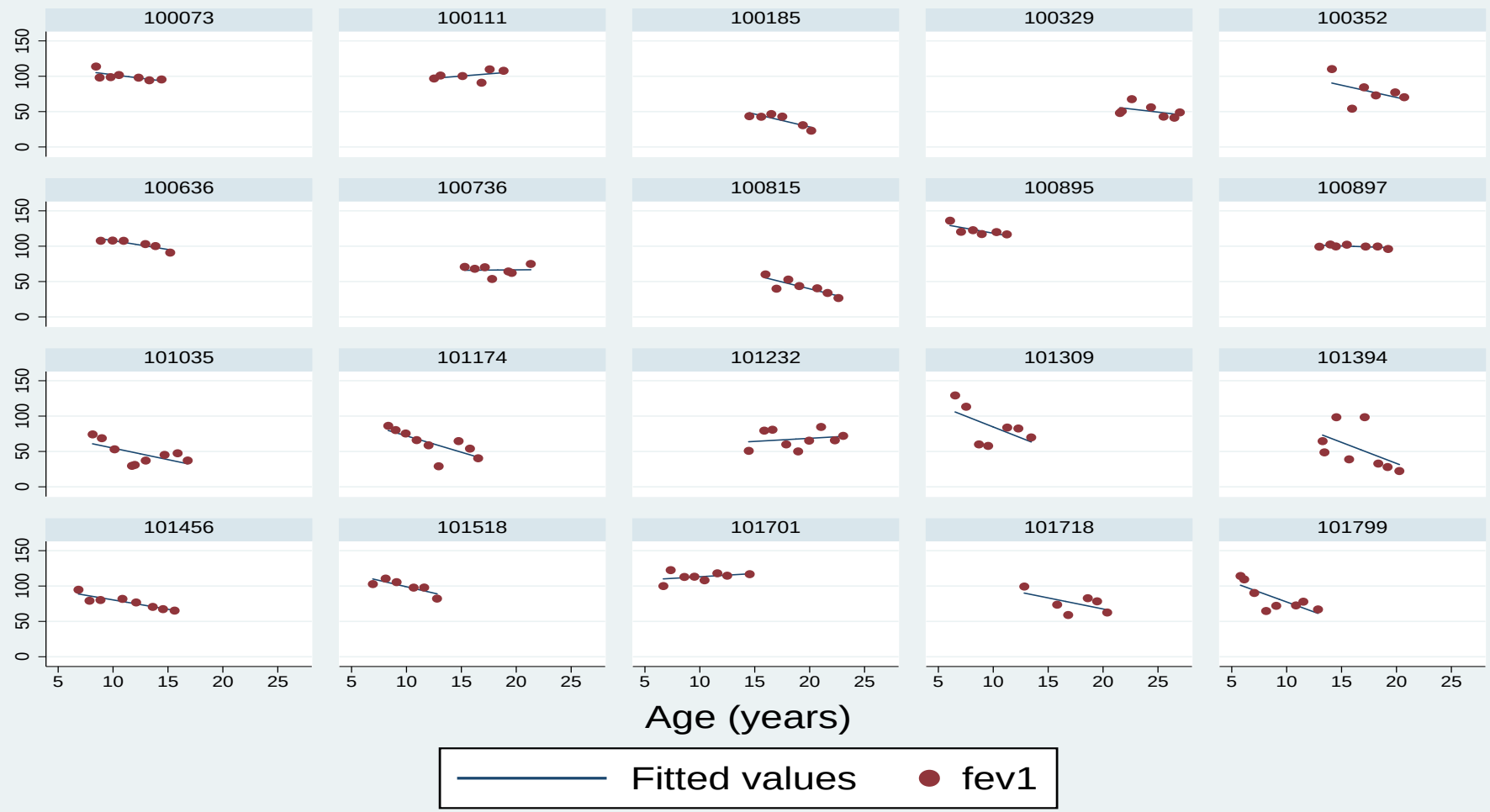
Results: CF Data – Individual Series



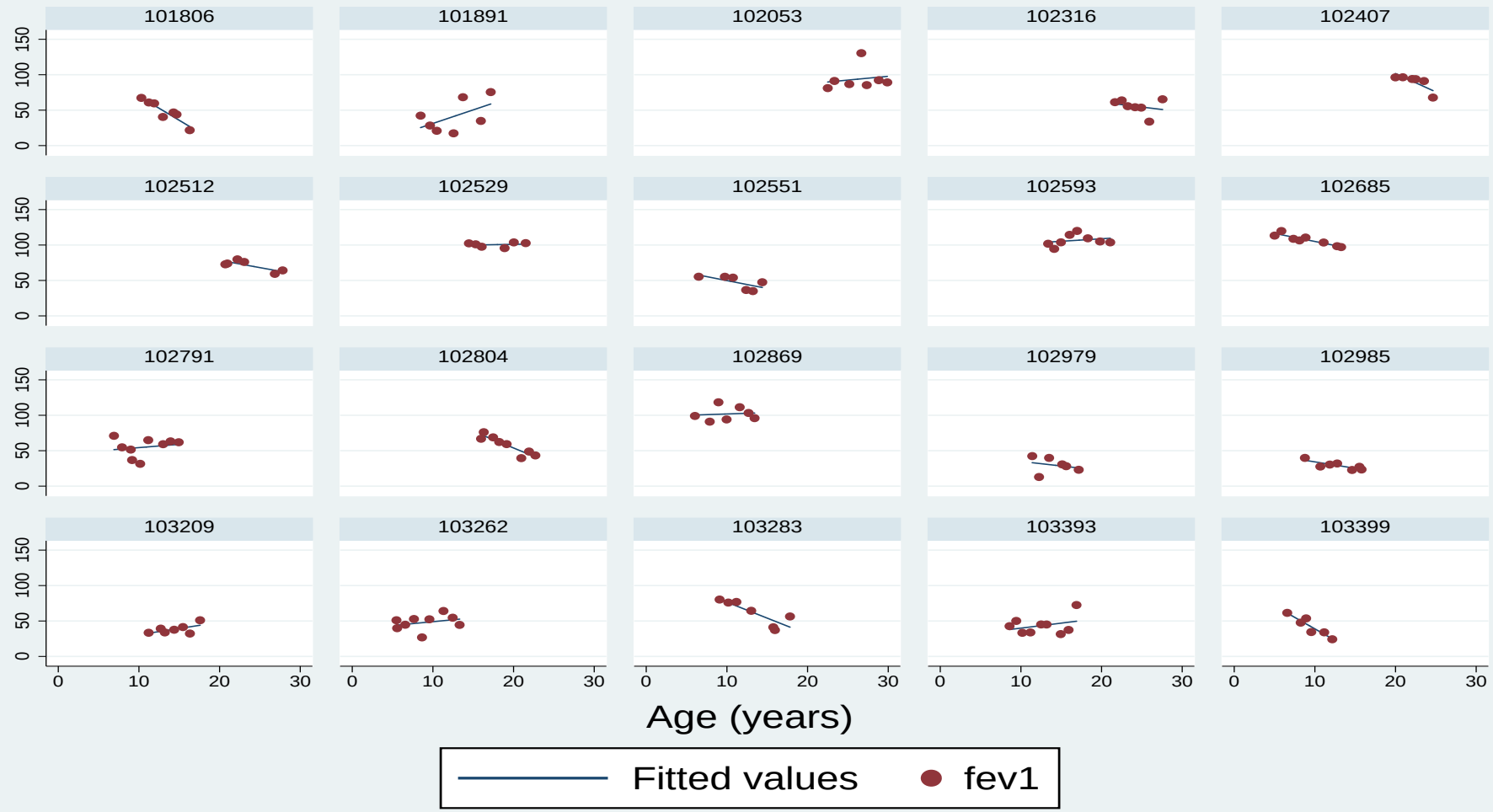
Results: CF Data – Individual Series



Results: CF Data – Fitted Lines



Results: CF Data – Fitted Lines



Derived Variable Analysis

- Create Summary for Each Subject
  - Mean outcome
  - Fitted Slope
- Analysis of Summaries
  - t-test or ANOVA for summary (e.g. slope)
  - Regression for summary (e.g. slope)
- Limitations
  - Different number of observations?
  - Different times of observation?
  - Additional adjustment?

Example: CF Data

```
*************************************************************
* cfkids-derived.do                                         *
*************************************************************
*                                                           *
* PURPOSE:  analysis of FEV1 among CF kids                  *
*                                                           *
* AUTHOR:  P. Heagerty                                      *
*                                                           *
* DATE:  31 March 2005                                      *
*************************************************************

use NewCFkids

***
*** save kid-level data
```

```
***

collapse (mean) f508 gender age0, by(id)

save KidData, replace

clear

***
*** fit a line to each child's data
***

use NewCFkids

sort id

**** can't estimate line if less than 2 observations
```

```
by id: drop if _N < 2

statsby "reg fev1 ageL" _b, by(id)

list in 1/10

***** merge back with the KidData

merge id using KidData


*****
***** summarize  b_ageL and b_cons by covariates
*****

sort gender
by gender: summarize b_ageL
ttest b_ageL, by(gender)
```

```
graph box b_ageL, over(gender)

sort f508
by f508: summarize b_ageL
xi: reg b_ageL i.f508
graph box b_ageL, over(f508)
```

Results: CF Data

```
. statsby "reg fev1 ageL" _b, by(id)

command:      reg fev1 ageL
statistics:   b_ageL     = _b[ageL]
              b_cons     = _b[_cons]
by:           id
.
. list in 1/10
     +-------------------------------+
     |     id      b_ageL     b_cons |
     |-------------------------------|
  1. | 100073   -1.936269   105.1512 |
  2. | 100111    1.245856   97.19055 |
  3. | 100185   -3.641983     48.351 |
  4. | 100329   -1.794132   55.53651 |
```

Results: CF Data

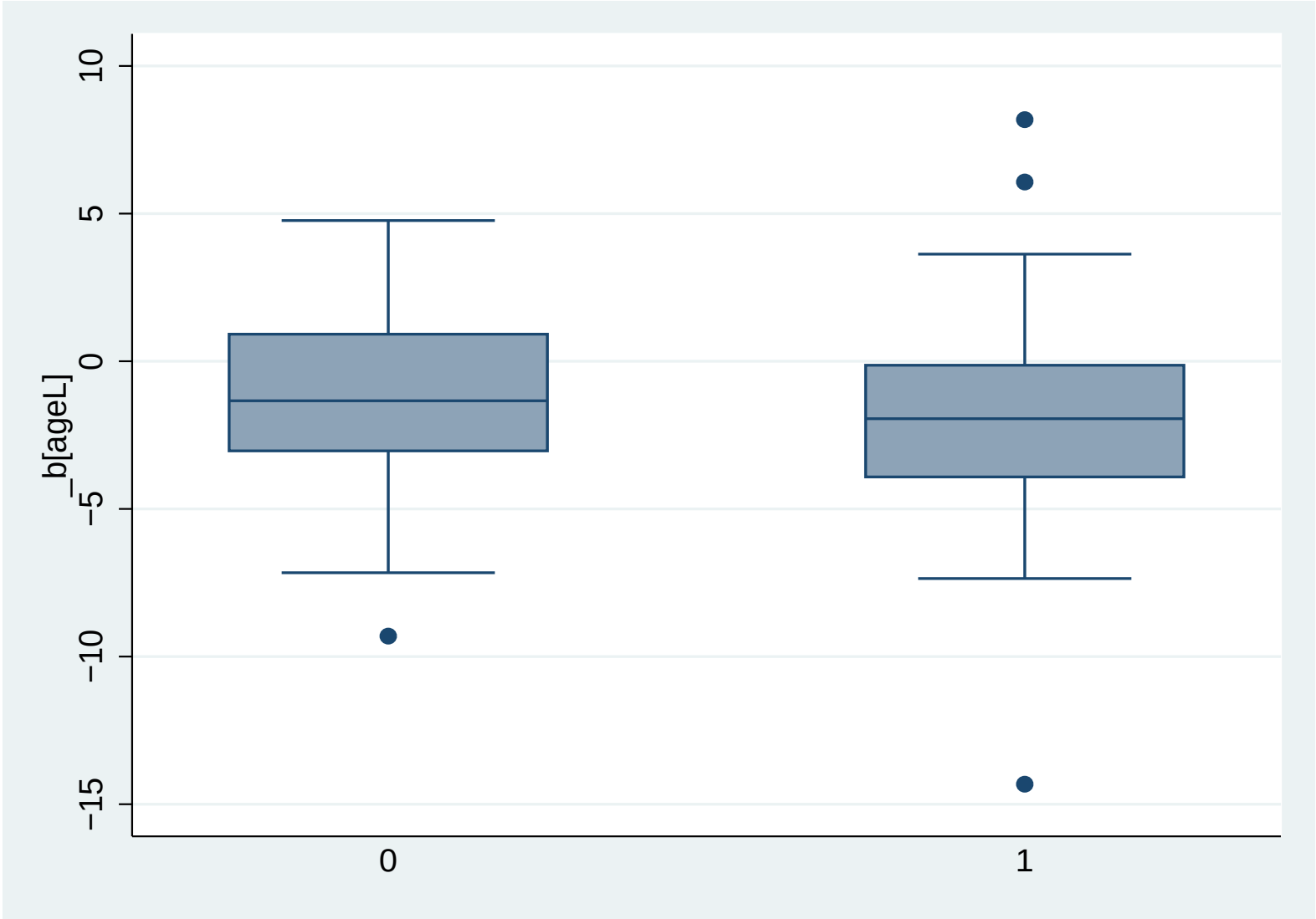
```
-------------------------------------------------------------------------------
-> gender = 0

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
      b_ageL |       102   -1.212864    2.703113   -9.30644   4.765747

-------------------------------------------------------------------------------
-> gender = 1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
      b_ageL |        98   -1.945086    3.063279  -14.32209   8.180941
```

Results: CF Data

```
. ttest b_ageL, by(gender)
Two-sample t test with equal variances
------------------------------------------------------------------------------
   Group |     Obs        Mean    Std. Err.   Std. Dev.   [95% Conf. Int.]
---------+--------------------------------------------------------------------
       0 |     102    -1.2128     .2676     2.7031    -1.7438   -0.6819
       1 |      98    -1.9450     .3094     3.0632    -2.5592   -1.3309
---------+--------------------------------------------------------------------
combined |     200    -1.5716     .2051     2.9012    -1.9761   -1.1671
---------+--------------------------------------------------------------------
    diff |              .73222     .4081                -0.0725    1.5370
------------------------------------------------------------------------------
Degrees of freedom: 198
```

```
                Ho: mean(0) - mean(1) = diff = 0

  Ha: diff < 0                Ha: diff != 0                Ha: diff > 0
    t =   1.7942                  t =   1.7942                  t =   1.7942
P < t =   0.9628            P > |t| =   0.0743            P > t =   0.0372
```

Results: CF Data – Slope Analysis



Results: CF Data

```
-------------------------------------------------------------------------------
-> f508 = 0

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
      b_ageL |        23   -.9898239    2.370343  -5.179185   3.831033

-------------------------------------------------------------------------------
-> f508 = 1

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
      b_ageL |        87   -1.482391    2.953235   -9.30644   6.069445
```

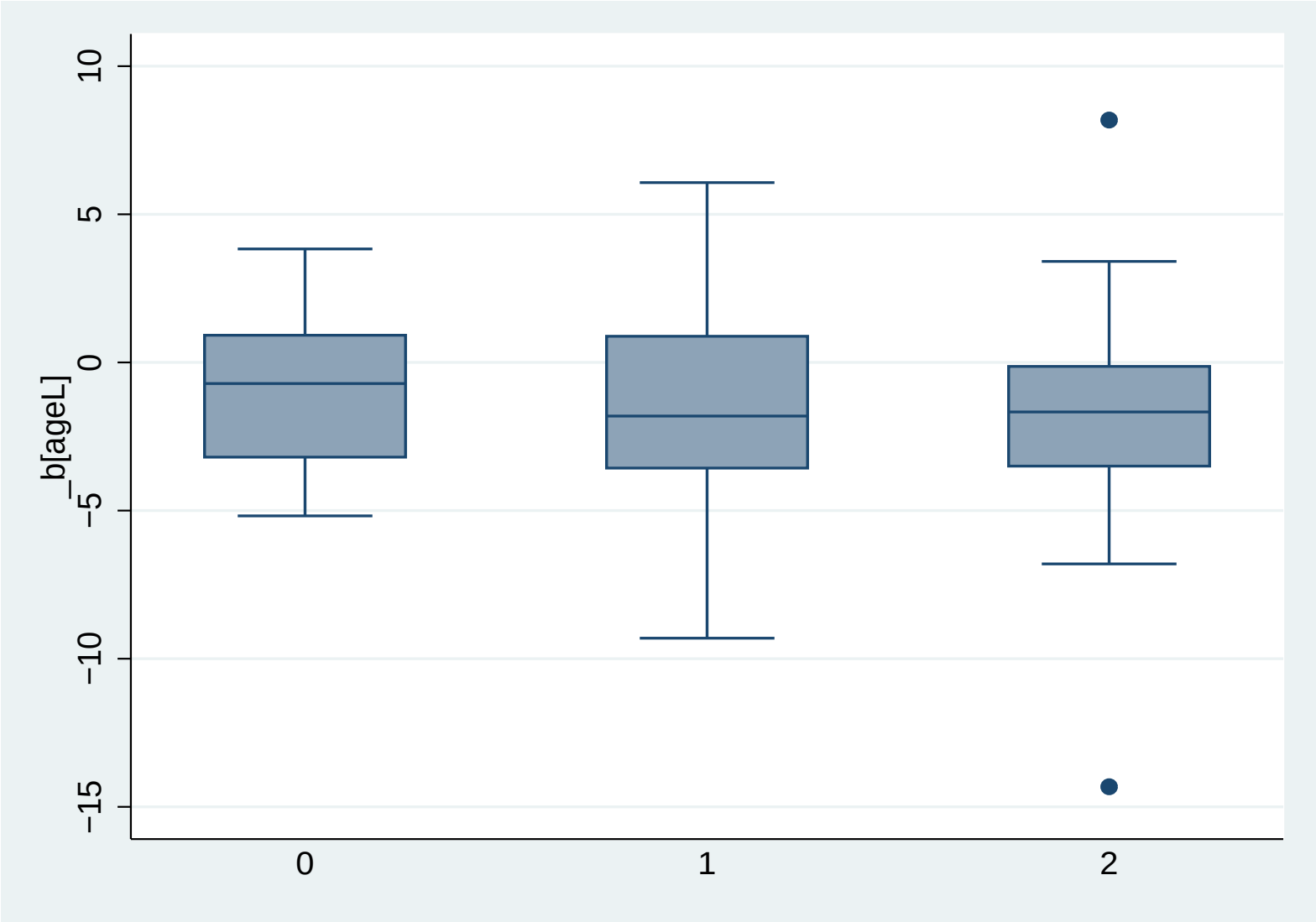
Results: CF Data

```
-------------------------------------------------------------------------------
-> f508 = 2

    Variable |       Obs        Mean    Std. Dev.       Min        Max
-------------+--------------------------------------------------------
      b_ageL |        90   -1.806628    2.975346  -14.32209   8.180941
```

Results: CF Data

```
. xi: reg b_ageL i.f508
      Source |       SS       df       MS              Number of obs =     200
-------------+------------------------------           F(  2,   197) =    0.80
       Model |  13.4484747     2  6.72423734            Prob > F      =  0.4520
    Residual |  1661.55371   197  8.43428277            R-squared     =  0.0080
-------------+------------------------------           Adj R-squared = -0.0020
       Total |  1675.00218   199  8.41709639            Root MSE      =  2.9042

------------------------------------------------------------------------------
     b_ageL |      Coef.   Std. Err.      t    P>|t|     [95% Conf. Interval]
------------+-----------------------------------------------------------------
  _If508_1 |    -0.4925     .6809    -0.72   0.470    -1.835      .8502
  _If508_2 |    -0.8168     .6785    -1.20   0.230    -2.154      .5213
     _cons |    -0.9898     .6055    -1.63   0.104    -2.184      .2043
------------------------------------------------------------------------------
```

Results: CF Data – Slope Analysis



Regression Analysis

- Linear Mixed Model
  - Random intercept
  - Random intercept and slope
- GEE
  - Independence correlation
  - Independence correlation with robust s.e.
  - Exchangeable correlation
  - Exchangeable correlation with robust s.e.

Regression Results: CF Data

```
*************************************************************
* cfkids-lmm-gee.do                                         *
*************************************************************
*                                                           *
* PURPOSE:  regression analysis of FEV1 among CF kids       *
*                                                           *
* AUTHOR:  P. Heagerty                                      *
*                                                           *
* DATE:  05 April 2005                                      *
*        04 April 2006                                      *
*************************************************************

use NewCFkids

***
```

```
*** create the interactions and dummy variables
***

gen f508_1 = (f508==1)
gen f508_2 = (f508==2)

gen ageXf508_1 = f508_1 * ageL
gen ageXf508_2 = f508_2 * ageL

gen ageXgender = gender * ageL

*****
***** Linear Mixed Model Analysis
*****



**************************************************
***  analysis using GLLAMM  (old; slow; general)            ***
```

```
*************************************************************

gen cons=1

eq int: cons
eq slope: ageL

set more off

*** Model 1:  Random Intercepts

gllamm fev1 age0 ageL gender f508_1 f508_2                          ///
             ageXgender ageXf508_1 ageXf508_2,                      ///
                        i(id) eqs(int) nrf(1) nip(10) adapt

*** Model 2:  Random Intercepts and Slopes

gllamm fev1 age0 ageL gender f508_1 f508_2                          ///
```

```
            ageXgender ageXf508_1 ageXf508_2,                    ///
                       i(id) eqs(int slope) nrf(2) nip(10) adapt

**************************************************
***  analysis using XTMIXED                    ***
**************************************************

*** Model 1:  Random Intercepts

xtmixed fev1 age0 ageL gender f508_1 f508_2                      ///
            ageXgender ageXf508_1 ageXf508_2     ||  id:

*** Model 2:  Random Intercepts and Slopes

xtmixed fev1 age0 ageL gender f508_1 f508_2                      ///
            ageXgender ageXf508_1 ageXf508_2     || id: ageL, cov(un)
```

```
*****
***** Generalized Estimating Equations Analysis
*****

xtgee fev1 age0 ageL gender f508_1 f508_2                          ///
           ageXgender ageXf508_1 ageXf508_2,                       ///
                      corr(independent) i(id)

xtcorr

xtgee fev1 age0 ageL gender f508_1 f508_2                         ///
           ageXgender ageXf508_1 ageXf508_2,                      ///
                      corr(independent) i(id) robust


xtgee fev1 age0 ageL gender f508_1 f508_2                        ///
           ageXgender ageXf508_1 ageXf508_2,                     ///
```

```
                        corr(exchangeable) i(id)

xtcorr

xtgee fev1 age0 ageL gender f508_1 f508_2                    ///
           ageXgender ageXf508_1 ageXf508_2,                 ///
                      corr(exchangeable) i(id) robust
```

Regression Results: CF Data – Random Intercepts

```
. gllamm fev1 age0 ageL gender f508_1 f508_2 ageXgender ageXf508_1 ageXf508_2
            i(id) eqs(int) nrf(1) nip(10) adapt

number of level 1 units = 1513    number of level 2 units = 200

log likelihood = -6255.0053
------------------------------------------------------------------------------
        fev1 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        age0 |   -1.8553    0.3300    -5.62   0.000     -2.5023    -1.2083
        ageL |   -0.5881    0.3924    -1.50   0.134     -1.3573     0.1810
      gender |   -1.1620    3.3575    -0.35   0.729     -7.7428     5.4187
      f508_1 |   -4.2822    5.5447    -0.77   0.440    -15.1498     6.5852
      f508_2 |   -6.7428    5.5759    -1.21   0.227    -17.6714     4.1857
ageXgender |   -0.8257    0.2490    -3.32   0.001     -1.3138    -0.3376
```

```
ageXf508_1 |  -0.4873   0.4218    -1.16   0.248    -1.3140    0.3394
ageXf508_2 |  -0.6568   0.4207    -1.56   0.118    -1.4814    0.1677
     _cons | 103.8077   6.6248    15.67   0.000    90.8231  116.7922
------------------------------------------------------------------------------

Variance at level 1
------------------------------------------------------------------------------

  148.32341 (5.7896206)

Variances and covariances of random effects
------------------------------------------------------------------------------
***level 2 (id)

    var(1): 497.48033 (51.806823)
------------------------------------------------------------------------------
```

Regression Results: CF Data – Random Int & Slopes

```
. gllamm fev1 age0 ageL gender f508_1 f508_2 ageXgender ageXf508_1 ageXf508_2
          i(id) eqs(int slope) nrf(2) nip(10) adapt

number of level 1 units = 1513     number of level 2 units = 200

log likelihood = -6202.1683
------------------------------------------------------------------------------
        fev1 |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        age0 |  -1.910407   .3283248    -5.82   0.000    -2.553912   -1.26690
        ageL |  -.6018747   .5839174    -1.03   0.303    -1.746332    .542582
      gender |  -1.296872   3.328747    -0.39   0.697    -7.821096    5.22735
      f508_1 |  -4.238208   5.495178    -0.77   0.441    -15.00856    6.53214
      f508_2 |  -6.655038   5.525834    -1.20   0.228    -17.48547    4.17539
  ageXgender |  -.7636477   .3770428    -2.03   0.043    -1.502638   -.024657
```

```
  ageXf508_1 |  -.5002841   .6288493    -0.80   0.426    -1.732806    .732237
  ageXf508_2 |  -.7450708   .6276375    -1.19   0.235    -1.975218     .48507
       _cons |   104.5162   6.572765    15.90   0.000     91.63378    117.398
------------------------------------------------------------------------------

Variance at level 1
------------------------------------------------------------------------------

  118.05247 (5.0252714)

Variances and covariances of random effects
------------------------------------------------------------------------------
***level 2 (id)

    var(1): 498.65795 (54.793715)
    cov(2,1): -7.2774328 (4.6057063) cor(2,1): -.15612915
    var(2): 4.3569809 (.73837017)
------------------------------------------------------------------------------
```

Regression Results: CF Data – Random Intercepts

```
. xtmixed fev1 age0 ageL gender f508_1 f508_2 ///
              ageXgender ageXf508_1 ageXf508_2     ||  id:

Mixed-effects REML regression          Number of obs      =      1513
Group variable: id                     Number of groups   =       200

Log restricted-likelihood =  -6249.041
------------------------------------------------------------------------------
        fev1 |   Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        age0 |  -1.855   0.3343    -5.55   0.000    -2.510   -1.200
        ageL |  -0.587   0.3930    -1.50   0.135    -1.358    0.182
      gender |  -1.162   3.3978    -0.34   0.732    -7.821    5.497
      f508_1 |  -4.280   5.6110    -0.76   0.445    -15.27    6.716
      f508_2 |  -6.740   5.6425    -1.19   0.232    -17.79    4.318
```

```
  ageXgender |  -0.825   0.2494    -3.31   0.001    -1.314   -0.336
  ageXf508_1 |  -0.487   0.4224    -1.15   0.248    -1.315    0.340
  ageXf508_2 |  -0.657   0.4213    -1.56   0.119    -1.483    0.168
       _cons | 103.806   6.7060    15.48   0.000    90.662  116.949
------------------------------------------------------------------------------
```

Regression Results: CF Data – Random Intercepts

```
------------------------------------------------------------------------------
  Random-effects Parameters  |   Estimate   Std. Err.  [95% Conf. Interval]
-----------------------------+------------------------------------------------
id: Identity                 |
                   sd(_cons) |   22.599    1.1906      20.382    25.057
-----------------------------+------------------------------------------------
                sd(Residual) |   12.197    0.2384      11.738    12.673
------------------------------------------------------------------------------
LR test vs. linear regression: chibar2(01) =  1554.17 Prob >= chibar2 = 0.0
```

Regression Results: CF Data – Random Int & Slopes

```
. xtmixed fev1 age0 ageL gender f508_1 f508_2 ///
              ageXgender ageXf508_1 ageXf508_2     || id: ageL, cov(un)

Mixed-effects REML regression                 Number of obs      =      1513
Group variable: id                            Number of groups   =       200

Log restricted-likelihood = -6194.5865
------------------------------------------------------------------------------
        fev1 |  Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
        age0 |  -1.910   0.3310    -5.77   0.000    -2.559   -1.261
        ageL |  -0.602   0.5902    -1.02   0.307    -1.759    0.554
      gender |  -1.300   3.3701    -0.39   0.700    -7.905    5.304
      f508_1 |  -4.238   5.5636    -0.76   0.446    -15.14    6.666
      f508_2 |  -6.652   5.5944    -1.19   0.234    -17.61    4.312
```

```
  ageXgender |  -0.762   0.3812    -2.00   0.045    -1.509   -0.015
  ageXf508_1 |  -0.500   0.6357    -0.79   0.431    -1.746    0.745
  ageXf508_2 |  -0.745   0.6344    -1.18   0.240    -1.989    0.497
       _cons | 104.519   6.6443    15.73   0.000    91.496  117.541
------------------------------------------------------------------------------
```

Regression Results: CF Data – Random Int & Slopes

Random-effects Parameters	Estimate	Std. Err.	[95% Conf.	Interval]
id: Unstructured				
sd(ageL)	2.124	0.1794	1.800	2.506
sd(_cons)	22.636	1.2560	20.303	25.237
corr(ageL,_cons)	-0.158	0.0921	-0.332	0.025
sd(Residual)	10.863	0.2312	10.419	11.326

LR test vs. linear regression: chi2(3) = 1663.08 Prob > chi2 = 0.00

Note: LR test is conservative and provided only for reference

Regression Results: CF Data – GEE Independence

```
. xtgee fev1 age0 ageL gender f508_1 f508_2 ageXgender ageXf508_1 ageXf508_2,
            corr(independent) i(id)

GEE population-averaged model          Number of obs      =      1513
Group variable:                   id   Number of groups   =       200
Link:                       identity   Obs per group: min =         6
Family:                     Gaussian                 avg =       7.6
Correlation:             independent                 max =         9
                                       Wald chi2(8)       =    248.46
Scale parameter:            636.1352   Prob > chi2        =    0.0000

Pearson chi2(1513):      962472.50     Deviance           = 962472.50
Dispersion (Pearson):    636.1352      Dispersion         =  636.1352
```

fev1	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
age0	-1.8614	0.1358	-13.71	0.000	-2.1276	-1.5952
ageL	-0.8910	0.7907	-1.13	0.260	-2.4409	0.6589
gender	-1.1329	2.2403	-0.51	0.613	-5.5239	3.2580
f508_1	-5.2795	3.7594	-1.40	0.160	-12.6478	2.0887
f508_2	-8.7756	3.7699	-2.33	0.020	-16.1646	-1.3865
ageXgender	-0.8187	0.5029	-1.63	0.104	-1.8045	0.1670
ageXf508_1	-0.1623	0.8505	-0.19	0.849	-1.8295	1.5047
ageXf508_2	-0.0393	0.8478	-0.05	0.963	-1.7009	1.6223
_cons	104.8027	3.9223	26.72	0.000	97.1151	112.4903

```
. xtcorr

Estimated within-id correlation matrix R:

        c1      c2      c3      c4      c5      c6      c7      c8      c9
r1  1.0000
r2  0.0000  1.0000
r3  0.0000  0.0000  1.0000
r4  0.0000  0.0000  0.0000  1.0000
r5  0.0000  0.0000  0.0000  0.0000  1.0000
r6  0.0000  0.0000  0.0000  0.0000  0.0000  1.0000
r7  0.0000  0.0000  0.0000  0.0000  0.0000  0.0000  1.0000
r8  0.0000  0.0000  0.0000  0.0000  0.0000  0.0000  0.0000  1.0000
r9  0.0000  0.0000  0.0000  0.0000  0.0000  0.0000  0.0000  0.0000  1.0000
```

Regression Results: CF Data – GEE Independence

```
. xtgee fev1 age0 ageL gender f508_1 f508_2 ageXgender ageXf508_1 ageXf508_2,
            corr(independent) i(id) robust

GEE population-averaged model          Number of obs      =      1513
Group variable:                   id   Number of groups   =       200
Link:                       identity   Obs per group: min =         6
Family:                     Gaussian                 avg =       7.6
Correlation:             independent                 max =         9
                                       Wald chi2(8)       =     70.80
Scale parameter:            636.1352   Prob > chi2        =    0.0000

Pearson chi2(1513):      962472.50     Deviance           = 962472.50
Dispersion (Pearson):       636.1352   Dispersion         =  636.1352
```

(standard errors adjusted for clustering on id)

fev1	Semi-robust Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
age0	-1.8614	0.3188	-5.84	0.000	-2.4864	-1.2364
ageL	-0.8910	0.6249	-1.43	0.154	-2.1159	0.3339
gender	-1.1329	3.4447	-0.33	0.742	-7.8845	5.6185
f508_1	-5.2795	6.0582	-0.87	0.384	-17.1536	6.5944
f508_2	-8.7756	6.1837	-1.42	0.156	-20.8955	3.3442
ageXgender	-0.8187	0.4545	-1.80	0.072	-1.7096	0.0721
ageXf508_1	-0.1623	0.6758	-0.24	0.810	-1.4870	1.1622
ageXf508_2	-0.0393	0.7010	-0.06	0.955	-1.4133	1.3347
_cons	104.8027	7.3461	14.27	0.000	90.4045	119.2009

Regression Results: CF Data – GEE Exchangeable

```
. xtgee fev1 age0 ageL gender f508_1 f508_2 ageXgender ageXf508_1 ageXf508_2,
            corr(exchangeable) i(id)

GEE population-averaged model          Number of obs      =      1513
Group variable:                   id   Number of groups   =       200
Link:                       identity   Obs per group: min =         6
Family:                     Gaussian                 avg =       7.6
Correlation:           exchangeable                 max =         9
                                       Wald chi2(8)       =    185.56
Scale parameter:           636.5125    Prob > chi2        =    0.0000
```

fev1	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
age0	-1.8553	0.3243	-5.72	0.000	-2.4911	-1.2195
ageL	-0.5896	0.4052	-1.46	0.146	-1.3838	0.2045
gender	-1.1619	3.3113	-0.35	0.726	-7.6519	5.3281
f508_1	-4.2875	5.4695	-0.78	0.433	-15.0076	6.4325
f508_2	-6.7531	5.5001	-1.23	0.220	-17.5332	4.0269
ageXgender	-0.8257	0.2571	-3.21	0.001	-1.3297	-0.3217
ageXf508_1	-0.4857	0.4355	-1.12	0.265	-1.3393	0.3679
ageXf508_2	-0.6537	0.4344	-1.50	0.132	-1.5051	0.1976
_cons	103.8126	6.5258	15.91	0.000	91.0221	116.6031

```
.
. xtcorr

Estimated within-id correlation matrix R:

        c1      c2      c3      c4      c5      c6      c7      c8      c9
r1  1.0000
r2  0.7515  1.0000
r3  0.7515  0.7515  1.0000
r4  0.7515  0.7515  0.7515  1.0000
r5  0.7515  0.7515  0.7515  0.7515  1.0000
r6  0.7515  0.7515  0.7515  0.7515  0.7515  1.0000
r7  0.7515  0.7515  0.7515  0.7515  0.7515  0.7515  1.0000
r8  0.7515  0.7515  0.7515  0.7515  0.7515  0.7515  0.7515  1.0000
r9  0.7515  0.7515  0.7515  0.7515  0.7515  0.7515  0.7515  0.7515  1.0000
```

Regression Results: CF Data – GEE Exchangeable

```
. xtgee fev1 age0 ageL gender f508_1 f508_2 ageXgender ageXf508_1 ageXf508_2,
          corr(exchangeable) i(id) robust

GEE population-averaged model          Number of obs      =      1513
Group variable:                  id    Number of groups   =       200
Link:                      identity    Obs per group: min =         6
Family:                    Gaussian                   avg =       7.6
Correlation:          exchangeable                    max =         9
                                       Wald chi2(8)       =     97.25
Scale parameter:           636.5125    Prob > chi2        =    0.0000
```

(standard errors adjusted for clustering on id)

fev1	Coef.	Semi-robust Std. Err.	z	P>|z|	[95% Conf.	Interval]
age0	-1.8553	0.3209	-5.78	0.000	-2.4844	-1.2261
ageL	-0.5896	0.5245	-1.12	0.261	-1.6176	0.4383
gender	-1.1619	3.3405	-0.35	0.728	-7.7093	5.3855
f508_1	-4.2875	5.9070	-0.73	0.468	-15.8651	7.2900
f508_2	-6.7531	5.9982	-1.13	0.260	-18.5095	5.0032
ageXgender	-0.8257	0.3715	-2.22	0.026	-1.5539	-0.0975
ageXf508_1	-0.4857	0.5798	-0.84	0.402	-1.6221	0.6507
ageXf508_2	-0.6537	0.5693	-1.15	0.251	-1.7697	0.4621
_cons	103.8126	7.2583	14.30	0.000	89.5865	118.0387

Summary – Regression Analysis

- Linear Mixed Models
  - Random effects used to model the subject-to-subject heterogeneity in trajectories.
  - Random effects model implies specific covariance forms (correlation).
  - Chosen model for random effects (between-subject) and the within-subject errors is used to:
    - Weight observations in order to estimate the regression parameters.
    - Provide standard errors for the regression parameters based on the implied correlation and variance model.

Summary – Regression Analysis

- GEE Analysis
  - The user directly chooses the correlation model.
  - Chosen model for correlation is used to:
    - Weight observations in order to estimate the regression parameters.
    - Provide standard errors for the regression parameters based on the assumed correlation and variance model.
  - **In addition**, a standard error estimate is calculated (if requested in STATA using `robust`) that is valid (correct) even if a poor correlation model was selected.