Biostatistics 140.655
Longitudinal Data Analysis
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Longitudinal GLM with GEE - Example

Pain Crossover Trial Data (Text page 13)

Binomial Outcome: % Patients Experiencing Relief on Different Drug Levels; P =Placebo, L = Low Analgesic, H = High Analgesic.

Data Coded Group-Wise:

visit	trt	group	rel	N
0	P	PLH	2	15
1	L	PLH	13	15
2	H	PLH	12	15
0	P	PHL	5	16
1	H	PHL	13	16
2	L	PHL	13	16
0	L	LPH	10	15
1	P	LPH	5	15
2	H	LPH	13	15
0	L	LHP	10	12
1	H	LHP	10	12
2	P	LHP	2	12
0	H	HPL	9	14
1	P	HPL	4	14
2	L	HPL	10	14
0	H	HLP	12	14
1	L	HLP	5	14
2	P	HLP	4	14

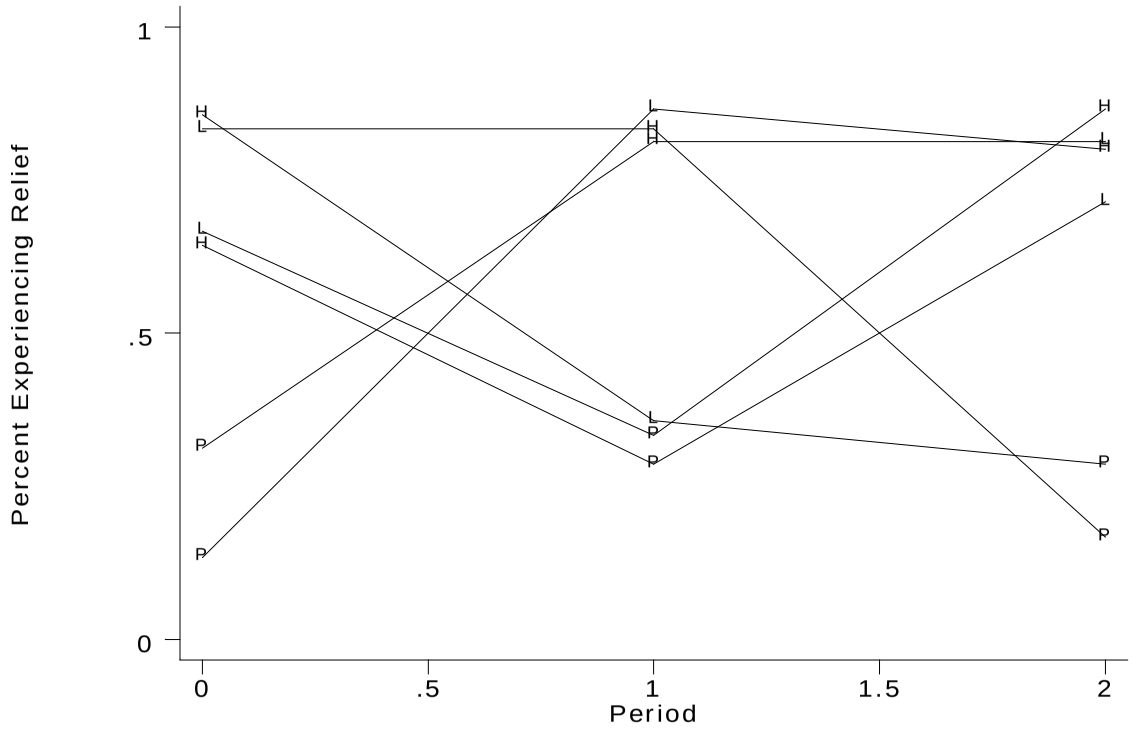
Data Summary by Treatment:

```
-> trt=P
Variable |     Obs        Mean    Std. Err.       [95% Conf. Interval]
---------+--------------------------------------------------------------
 centrel |       6      .252877    .0336192         .166456     .339298

-> trt=L
Variable |     Obs        Mean    Std. Err.       [95% Conf. Interval]
---------+--------------------------------------------------------------
 centrel |       6     .7084325    .0767358         .511177    .9056881

-> trt=H
Variable |     Obs        Mean    Std. Err.       [95% Conf. Interval]
---------+--------------------------------------------------------------
 centrel |       6     .8020833    .0334888        .7159977     .888169
```

Pain Scores connected by Group:



Logistic Regression Using Gee (Stata)

Recommended Syntax:
xtgee outcome predictors, fam(bin N) link(logit) corr(?) robust eform

Unstructured Correlation:

```
xtgee rel low high, i(group) fam(binomial N) link(logit) robust eform corr(uns)

GEE population-averaged model                   Number of obs      =        18
Group and time vars:           group visit      Number of groups   =         6
Link:                                logit      Obs per group: min =         3
Family:                           binomial                     avg =       3.0
Correlation:                   unstructured                     max =         3
                                                Wald chi2(2)       =     79.44
Scale parameter:                         1      Prob > chi2        =    0.0000

                            (standard errors adjusted for clustering on group)
------------------------------------------------------------------------------
             |             Semi-robust
         rel | Odds Ratio   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
         low |   6.936206   3.477014      3.864   0.000       2.596735    18.52748
        high |     10.527   2.996396      8.270   0.000        6.02586    18.39034
------------------------------------------------------------------------------


. xtcorr

Estimated within-group correlation matrix R:

         c1       c2       c3
r1   1.0000
r2  -0.4829   1.0000
r3  -0.0837  -0.0058   1.0000
```

Independent Correlation:

```
. xtgee rel low high, i(group) fam(binomial N) link(logit) robust eform corr(ind)

GEE population-averaged model                   Number of obs      =        18
Group variable:                      group      Number of groups   =         6
Link:                                logit      Obs per group: min =         3
Family:                           binomial                     avg =       3.0
Correlation:                   independent                     max =         3
                                                Wald chi2(2)       =     87.20
Scale parameter:                         1      Prob > chi2        =    0.0000

Pearson chi2(15):                    17.62      Deviance           =     17.01
Dispersion (Pearson):              1.17472      Dispersion         =  1.134261

                           (standard errors adjusted for clustering on group)
------------------------------------------------------------------------------
             |             Semi-robust
         rel | Odds Ratio   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
         low |   7.098182    3.37147      4.126   0.000       2.797991    18.00727
        high |   11.80749   3.148445      9.258   0.000        7.00142    19.91264
------------------------------------------------------------------------------

.
. xtcorr

Estimated within-group correlation matrix R:

        c1      c2      c3
r1  1.0000
r2  0.0000  1.0000
r3  0.0000  0.0000  1.0000
```

Exchangeable Correlation:

```
. xtgee rel low high, i(group) fam(binomial N) link(logit) robust eform corr(ex
> ch) nolog

GEE population-averaged model                   Number of obs      =        18
Group variable:                       group     Number of groups   =         6
Link:                                 logit     Obs per group: min =         3
Family:                           binomial                    avg =       3.0
Correlation:                  exchangeable                    max =         3
                                                Wald chi2(2)       =     87.20
Scale parameter:                         1      Prob > chi2        =    0.0000

                           (standard errors adjusted for clustering on group)
------------------------------------------------------------------------------
             |             Semi-robust
         rel | Odds Ratio   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
         low |   7.098182    3.37147      4.126   0.000       2.797991    18.00727
        high |   11.80749   3.148445      9.258   0.000        7.00142    19.91264
------------------------------------------------------------------------------

. xtcorr

Estimated within-group correlation matrix R:

            c1       c2       c3
r1     1.0000
r2    -0.2293   1.0000
r3    -0.2293  -0.2293   1.0000
```

AR1 Correlation:

```
. xtgee rel low high, i(group) fam(binomial N) link(logit) robust eform corr(ar
> 1) nolog

GEE population-averaged model                   Number of obs      =        18
Group and time vars:           group visit      Number of groups   =         6
Link:                                logit      Obs per group: min =         3
Family:                           binomial                     avg =       3.0
Correlation:                         AR(1)                     max =         3
                                                Wald chi2(2)       =    101.86
Scale parameter:                          1     Prob > chi2        =    0.0000

                           (standard errors adjusted for clustering on group)
------------------------------------------------------------------------------
             |             Semi-robust
         rel | Odds Ratio   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
         low |   7.998766   3.664069      4.539   0.000       3.259157    19.63093
        high |   14.13425   3.728974     10.039   0.000        8.42761    23.70508
------------------------------------------------------------------------------

. xtcorr

Estimated within-group correlation matrix R:

            c1       c2       c3
r1     1.0000
r2    -0.4081   1.0000
r3     0.1666  -0.4081   1.0000
```

Prediction: See xtpred

Time Effect?

```
. xtgee rel low high visit, i(group) fam(binomial N) link(logit) robust eform n
> olog

GEE population-averaged model                   Number of obs      =        18
Group variable:                      group      Number of groups   =         6
Link:                                logit      Obs per group: min =         3
Family:                           binomial                     avg =       3.0
Correlation:                   exchangeable                     max =         3
                                                Wald chi2(3)       =    183.22
Scale parameter:                         1      Prob > chi2        =    0.0000

                            (standard errors adjusted for clustering on group)
------------------------------------------------------------------------------
                             |             Semi-robust
         rel | Odds Ratio   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
         low |   7.081076   3.244466      4.272   0.000       2.884621     17.3824
        high |   11.72768   3.025567      9.543   0.000       7.073182    19.44507
       visit |   1.109239   .1526732      0.753   0.451       .8469697    1.452723
------------------------------------------------------------------------------
```

Example Results Robust to respecification of Correlation, Time Effect – But more Exploration Advised.

Effect Modification via Time?

```
. gen lvisit = low*visit

. gen hvisit = high*visit

. xtgee rel low high visit lvisit hvisit, i(group) fam(binomial N) link(logit)
> robust eform nolog

GEE population-averaged model                   Number of obs      =        18
Group variable:                      group      Number of groups   =         6
Link:                                logit      Obs per group: min =         3
Family:                           binomial                     avg =       3.0
Correlation:                   exchangeable                     max =         3
                                                Wald chi2(4)       =    283.95
Scale parameter:                         1      Prob > chi2        =    0.0000

                            (standard errors adjusted for clustering on group)
------------------------------------------------------------------------------
                             |             Semi-robust
         rel | Odds Ratio   Std. Err.       z     P>|z|       [95% Conf. Interval]
-------------+----------------------------------------------------------------
         low |    5.82417   3.942285      2.603   0.009       1.545503    21.94817
        high |   6.026568   2.161505      5.008   0.000       2.983842    12.17206
       visit |   .8601037   .1587488     -0.817   0.414       .5990252     1.23497
      lvisit |   1.227045   .3728156      0.673   0.501       .6764537    2.225783
      hvisit |   2.035484   .6409025      2.257   0.024       1.098131    3.772952
------------------------------------------------------------------------------
```