**data** epileptic\_w;

input ID TRT Age C0 C1 C2 C3 C4;

datalines;

1 0 31 11 5 3 3 3

2 0 30 11 3 5 3 3

………………………..

59 1 37 12 1 4 3 2

;

**run**;

**data** epileptic;

set epileptic\_w;

array AC(**1**:**5**) C0-C4;

array Aweek(**1**:**5**) (**0** **2** **4** **6** **8**);

do i=**1** to **5**;

Count = AC[i];

week = Aweek[i];

L\_per = log(**2**);

if i eq **1** then L\_per=log(**8**);

output;

end;

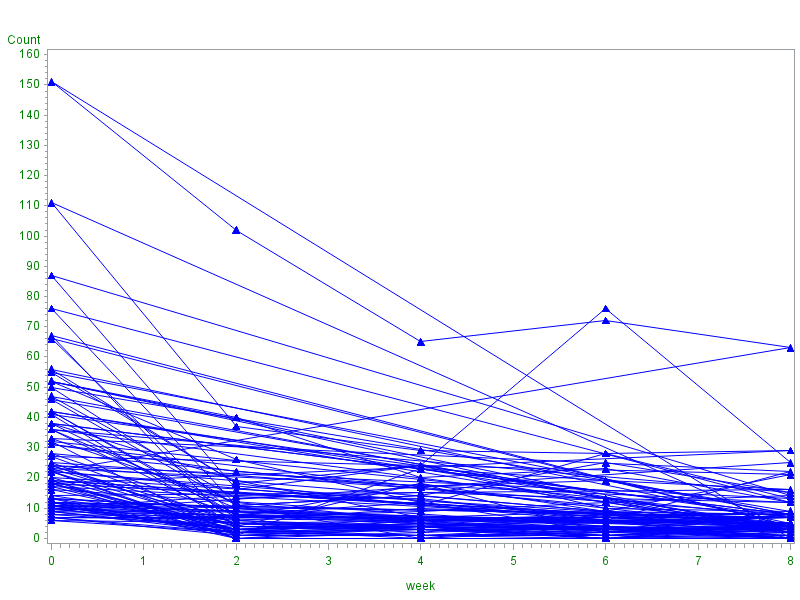
drop C0-C4 Aweek1 - Aweek5 i;

**run**;

**proc** **print** data=epileptic (obs=**10**);

**run**;

| **Obs** | **ID** | **TRT** | **Age** | **Count** | **week** | **L\_per** |
| --- | --- | --- | --- | --- | --- | --- |
| **1** | 1 | 0 | 31 | 11 | 0 | 2.07944 |
| **2** | 1 | 0 | 31 | 5 | 2 | 0.69315 |
| **3** | 1 | 0 | 31 | 3 | 4 | 0.69315 |
| **4** | 1 | 0 | 31 | 3 | 6 | 0.69315 |
| **5** | 1 | 0 | 31 | 3 | 8 | 0.69315 |
| **6** | 2 | 0 | 30 | 11 | 0 | 2.07944 |
| **7** | 2 | 0 | 30 | 3 | 2 | 0.69315 |
| **8** | 2 | 0 | 30 | 5 | 4 | 0.69315 |
| **9** | 2 | 0 | 30 | 3 | 6 | 0.69315 |
| **10** | 2 | 0 | 30 | 3 | 8 | 0.69315 |



**proc** **glimmix** data=epileptic;

class ID trt (ref='0');

model Count = week trt week\*trt/d=poisson link=log offset=L\_per solution;

random intercept week/subject=ID type=UN G;

**run**;

**quit**;

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.EPILEPTIC |
| **Response Variable** | Count |
| **Response Distribution** | Poisson |
| **Link Function** | Log |
| **Variance Function** | Default |
| **Offset Variable** | L\_per |
| **Variance Matrix Blocked By** | ID |
| **Estimation Technique** | Residual PL |
| **Degrees of Freedom Method** | Containment |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 59 | 1 2 3 4 5 ……. 59 |
| **TRT** | 2 | 1 0 |

|  |  |
| --- | --- |
| **Number of Observations Read** | 295 |
| **Number of Observations Used** | 295 |

| **Dimensions** | |
| --- | --- |
| **G-side Cov. Parameters** | 3 |
| **Columns in X** | 6 |
| **Columns in Z per Subject** | 2 |
| **Subjects (Blocks in V)** | 59 |
| **Max Obs per Subject** | 5 |

| **Optimization Information** | |
| --- | --- |
| **Optimization Technique** | Dual Quasi-Newton |
| **Parameters in Optimization** | 3 |
| **Lower Boundaries** | 2 |
| **Upper Boundaries** | 0 |
| **Fixed Effects** | Profiled |
| **Starting From** | Data |

| **Iteration History** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Iteration** | **Restarts** | **Subiterations** | **Objective Function** | **Change** | **Max Gradient** |
| **0** | **0** | **5** | 715.90199832 | 2.00000000 | 0.141681 |
| **1** | **0** | **6** | 790.0318566 | 0.25874549 | 0.00005 |
| **2** | **0** | **5** | 799.18843282 | 0.00762797 | 0.000969 |
| **18** | **0** | **1** | 799.46552535 | 0.00000026 | 0.000155 |
| **19** | **0** | **1** | 799.46552774 | 0.00000463 | 0.001866 |

|  |
| --- |
| Did not converge. |

**proc** **glimmix** data=epileptic method=quad(QPOINTS=**5**);

class ID trt (ref='0');

model Count = week trt week\*trt/d=poisson link=log offset=L\_per solution;

random intercept week/subject=ID type=UN G;

**run**;

**quit**;

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.EPILEPTIC |
| **Response Variable** | Count |
| **Response Distribution** | Poisson |
| **Link Function** | Log |
| **Variance Function** | Default |
| **Offset Variable** | L\_per |
| **Variance Matrix Blocked By** | ID |
| **Estimation Technique** | Maximum Likelihood |
| **Likelihood Approximation** | Gauss-Hermite Quadrature |
| **Degrees of Freedom Method** | Containment |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 59 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 |
| **TRT** | 2 | 1 0 |

|  |  |
| --- | --- |
| **Number of Observations Read** | 295 |
| **Number of Observations Used** | 295 |

| **Dimensions** | |
| --- | --- |
| **G-side Cov. Parameters** | 3 |
| **Columns in X** | 6 |
| **Columns in Z per Subject** | 2 |
| **Subjects (Blocks in V)** | 59 |
| **Max Obs per Subject** | 5 |

| **Optimization Information** | |
| --- | --- |
| **Optimization Technique** | Dual Quasi-Newton |
| **Parameters in Optimization** | 7 |
| **Lower Boundaries** | 2 |
| **Upper Boundaries** | 0 |
| **Fixed Effects** | Not Profiled |
| **Starting From** | GLM estimates |
| **Quadrature Points** | 5 |

| **Iteration History** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Iteration** | **Restarts** | **Evaluations** | **Objective Function** | **Change** | **Max Gradient** |
| **0** | **0** | 4 | 1935.877681 | . | 1360.217 |
| **1** | **0** | 5 | 1934.0660428 | 1.81163821 | 1278.973 |
| **2** | **0** | 5 | 1931.4844275 | 2.58161522 | 1243.717 |
| **3** | **0** | 5 | 1929.8241138 | 1.66031377 | 1179.902 |
| **4** | **0** | 5 | 1920.0003502 | 9.82376352 | 491.0731 |
| **5** | **0** | 3 | 1913.8175124 | 6.18283779 | 1285.27 |
| **6** | **0** | 3 | 1912.8773189 | 0.94019352 | 674.922 |
| **7** | **0** | 4 | 1910.8501449 | 2.02717403 | 497.4587 |
| **8** | **0** | 5 | 1910.4180459 | 0.43209903 | 192.8727 |
| **9** | **0** | 2 | 1909.983809 | 0.43423687 | 54.65148 |
| **10** | **0** | 3 | 1909.915481 | 0.06832802 | 45.72635 |
| **11** | **0** | 3 | 1909.8969513 | 0.01852967 | 26.35039 |
| **12** | **0** | 3 | 1909.8935545 | 0.00339679 | 4.640038 |
| **13** | **0** | 3 | 1909.8931368 | 0.00041772 | 6.534372 |
| **14** | **0** | 3 | 1909.8930695 | 0.00006733 | 0.209633 |
| **15** | **0** | 3 | 1909.8930693 | 0.00000021 | 0.00327 |

|  |
| --- |
| Convergence criterion (GCONV=1E-8) satisfied. |

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | 1909.89 |
| **AIC (smaller is better)** | 1923.89 |
| **AICC (smaller is better)** | 1924.28 |
| **BIC (smaller is better)** | 1938.44 |
| **CAIC (smaller is better)** | 1945.44 |
| **HQIC (smaller is better)** | 1929.57 |

| **Fit Statistics for Conditional Distribution** | |
| --- | --- |
| **-2 log L(Count | r. effects)** | 1562.24 |
| **Pearson Chi-Square** | 472.31 |
| **Pearson Chi-Square / DF** | 1.60 |

| **Estimated G Matrix** | | | |
| --- | --- | --- | --- |
| **Effect** | **Row** | **Col1** | **Col2** |
| Intercept | **1** | 0.5277 | 0.01120 |
| week | **2** | 0.01120 | 0.005059 |

| **Covariance Parameter Estimates** | | | |
| --- | --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** | **Standard Error** |
| **UN(1,1)** | ID | 0.5277 | 0.1045 |
| **UN(2,1)** | ID | 0.01120 | 0.008762 |
| **UN(2,2)** | ID | 0.005059 | 0.001461 |

| **Solutions for Fixed Effects** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **TRT** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** |  | 1.1039 | 0.1428 | 57 | 7.73 | <.0001 |
| **week** |  | -0.01133 | 0.01692 | 57 | -0.67 | 0.5057 |
| **TRT** | 1 | 0.01755 | 0.1966 | 177 | 0.09 | 0.9290 |
| **TRT** | 0 | 0 | . | . | . | . |
| **week\*TRT** | 1 | -0.04675 | 0.02350 | 177 | -1.99 | 0.0482 |
| **week\*TRT** | 0 | 0 | . | . | . | . |

| **Type III Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **week** | 1 | 57 | 8.09 | 0.0062 |
| **TRT** | 1 | 177 | 0.01 | 0.9290 |
| **week\*TRT** | 1 | 177 | 3.96 | 0.0482 |

**proc** **glimmix** data=epileptic method=quad(QPOINTS=**20**);

class ID trt (ref='0');

model Count = week trt week\*trt/d=poisson link=log offset=L\_per solution;

random intercept week/subject=ID type=UN G;

**run**;

**quit**;

| **Solutions for Fixed Effects** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **TRT** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** |  | 1.1039 | 0.1428 | 57 | 7.73 | <.0001 |
| **week** |  | -0.01133 | 0.01692 | 57 | -0.67 | 0.5058 |
| **TRT** | 1 | 0.01755 | 0.1966 | 177 | 0.09 | 0.9290 |
| **TRT** | 0 | 0 | . | . | . | . |
| **week\*TRT** | 1 | -0.04675 | 0.02351 | 177 | -1.99 | 0.0482 |
| **week\*TRT** | 0 | 0 | . | . | . | . |

**proc** **glimmix** data=epileptic method=quad(QPOINTS=**50**);

class ID trt (ref='0');

model Count = week trt week\*trt/d=poisson link=log offset=L\_per solution;

random intercept week/subject=ID type=UN G;

**run**;

**quit**;

| **Solutions for Fixed Effects** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **TRT** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** |  | 1.1039 | 0.1428 | 57 | 7.73 | <.0001 |
| **week** |  | -0.01133 | 0.01692 | 57 | -0.67 | 0.5058 |
| **TRT** | 1 | 0.01755 | 0.1966 | 177 | 0.09 | 0.9290 |
| **TRT** | 0 | 0 | . | . | . | . |
| **week\*TRT** | 1 | -0.04675 | 0.02351 | 177 | -1.99 | 0.0482 |
| **week\*TRT** | 0 | 0 | . | . | . | . |

**The negative binomial model is an alternative to the Poisson model. The interpretation is similar, and it allow for overdispersion. In the negative binomial model** var(Y)=μ+kμ2

**proc** **glimmix** data=epileptic method=quad(QPOINTS=**20**);

class ID trt (ref='0');

model Count = week trt week\*trt/d=negbin link=log offset=L\_per solution;

random intercept week/subject=ID type=UN G;

**run**;

**quit**;

|  |
| --- |
| The SAS System |

The GLIMMIX Procedure

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.EPILEPTIC |
| **Response Variable** | Count |
| **Response Distribution** | Negative Binomial |
| **Link Function** | Log |
| **Variance Function** | Default |
| **Offset Variable** | L\_per |
| **Variance Matrix Blocked By** | ID |
| **Estimation Technique** | Maximum Likelihood |
| **Likelihood Approximation** | Gauss-Hermite Quadrature |
| **Degrees of Freedom Method** | Containment |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 59 | 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 |
| **TRT** | 2 | 1 0 |

|  |  |
| --- | --- |
| **Number of Observations Read** | 295 |
| **Number of Observations Used** | 295 |

| **Dimensions** | |
| --- | --- |
| **G-side Cov. Parameters** | 3 |
| **R-side Cov. Parameters** | 1 |
| **Columns in X** | 6 |
| **Columns in Z per Subject** | 2 |
| **Subjects (Blocks in V)** | 59 |
| **Max Obs per Subject** | 5 |

| **Optimization Information** | |
| --- | --- |
| **Optimization Technique** | Dual Quasi-Newton |
| **Parameters in Optimization** | 8 |
| **Lower Boundaries** | 3 |
| **Upper Boundaries** | 0 |
| **Fixed Effects** | Not Profiled |
| **Starting From** | GLM estimates |
| **Quadrature Points** | 20 |

| **Iteration History** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Iteration** | **Restarts** | **Evaluations** | **Objective Function** | **Change** | **Max Gradient** |
| **0** | **0** | 4 | 1864.9791757 | . | 1322.935 |
| **1** | **0** | 5 | 1863.4623877 | 1.51678805 | 1357.649 |
| **61** | **0** | 3 | 1773.992202 | 0.00000511 | 1021.949 |

|  |
| --- |
| Convergence criterion (GCONV=1E-8) satisfied. |

| **Fit Statistics** | |
| --- | --- |
| **-2 Log Likelihood** | 1773.99 |
| **AIC (smaller is better)** | 1789.99 |
| **AICC (smaller is better)** | 1790.50 |
| **BIC (smaller is better)** | 1806.61 |
| **CAIC (smaller is better)** | 1814.61 |
| **HQIC (smaller is better)** | 1796.48 |

| **Fit Statistics for Conditional Distribution** | |
| --- | --- |
| **-2 log L(Count | r. effects)** | 1570.51 |
| **Pearson Chi-Square** | 227.57 |
| **Pearson Chi-Square / DF** | 0.77 |

| **Estimated G Matrix** | | | |
| --- | --- | --- | --- |
| **Effect** | **Row** | **Col1** | **Col2** |
| **Intercept** | **1** | 0.5610 | 0.04230 |
| **week** | **2** | 0.04230 | 0.003190 |

| **Covariance Parameter Estimates** | | | |
| --- | --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** | **Standard Error** |
| **UN(1,1)** | **ID** | 0.5610 | 0.1585 |
| **UN(2,1)** | **ID** | 0.04230 | 0.01823 |
| **UN(2,2)** | **ID** | 0.003190 | 0.003409 |
| **Scale** |  | **0.1407** | **0.02871** |

| **Solutions for Fixed Effects** | | | | | | |
| --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **TRT** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** |  | 1.1728 | 0.1586 | 57 | 7.40 | <.0001 |
| **week** |  | -0.02103 | 0.01921 | 57 | -1.09 | 0.2782 |
| **TRT** | **1** | -0.01187 | 0.2179 | 177 | -0.05 | 0.9566 |
| **TRT** | **0** | 0 | . | . | . | . |
| **week\*TRT** | **1** | -0.04466 | 0.02665 | 177 | -1.68 | 0.0955 |
| **week\*TRT** | **0** | 0 | . | . | . | . |

| **Type III Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **week** | 1 | 57 | 9.50 | 0.0032 |
| **TRT** | 1 | 177 | 0.00 | 0.9566 |
| **week\*TRT** | 1 | 177 | 2.81 | 0.0955 |

\*Example - Schizophrenia

Data analyzed by Hedeker and Gibbons (1997). A randomized trial for schizophrenia. The trial contained

312 patients received drug therapy and 101 received placebo. The measurements were taken at weeks 0, 1, 3, 6,

but some subjects have missing data due to dropout. The outcome of interest is severity of illness (1 = normal, ... , 7 = extremely ill);

**data** schizo;

input ID Group week severity;

sqrtweek = week\*\*(**0.5**);

r\_severity = round(severity);

datalines;

1103 1 0 5.5

1103 1 1 3.0

1103 1 3 2.5

1103 1 6 4.0

……………………………

9316 0 0 5.5

9316 0 1 6.0

9316 0 3 6.5

9316 0 6 6.0

**run**;

**proc** **freq** data=schizo;

tables group\*week;

**run**;

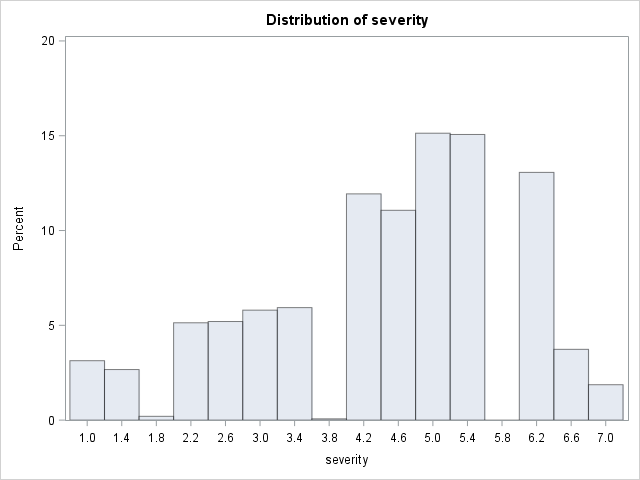
| **Table of Group by week** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Group** | **week** | | | | |
| **Frequency Percent Row Pct Col Pct** | **0** | **1** | **3** | **6** | **Total** |
| **0** | 101 6.11 25.00 24.46 | 101 6.11 25.00 24.46 | 101 6.11 25.00 24.46 | 101 6.11 25.00 24.46 | 404 24.46 |
| **1** | 312 18.89 25.00 75.54 | 312 18.89 25.00 75.54 | 312 18.89 25.00 75.54 | 312 18.89 25.00 75.54 | 1248 75.54 |
| **Total** | 413 25.00 | 413 25.00 | 413 25.00 | 413 25.00 | 1652 100.00 |

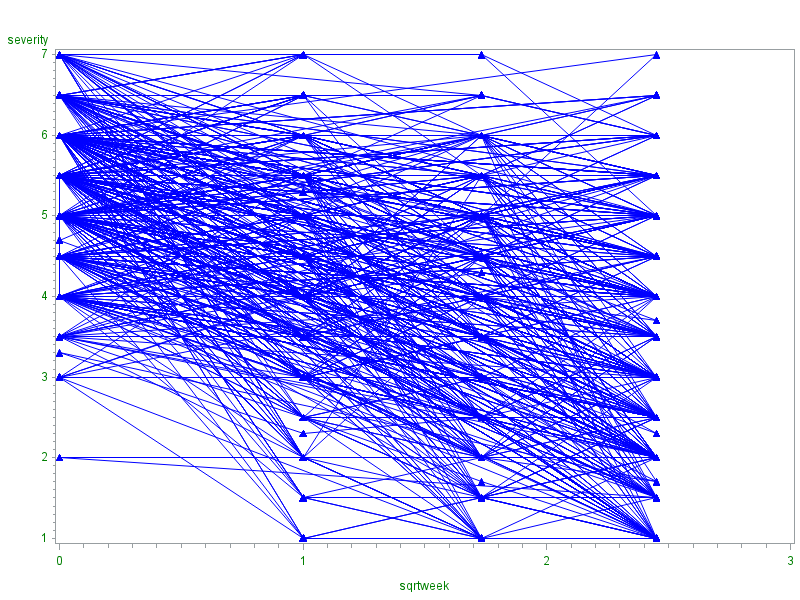
**proc** **univariate** data=schizo;

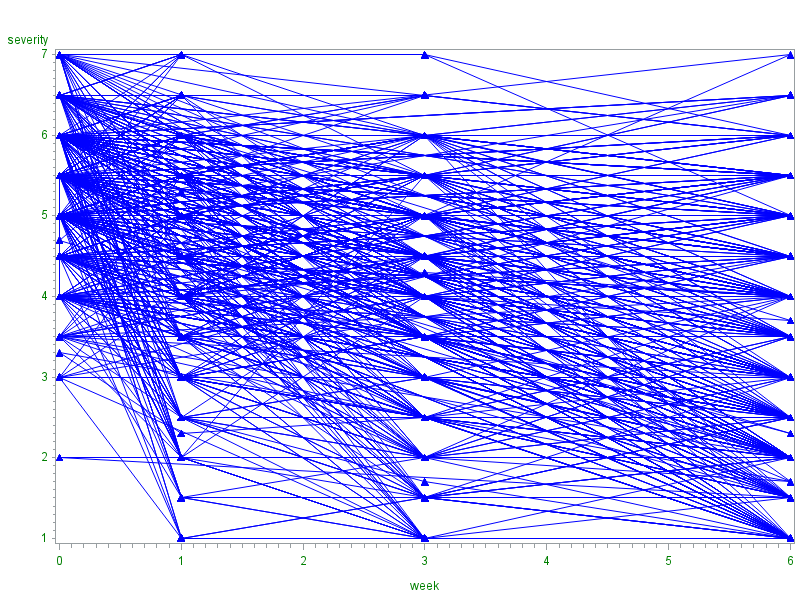
var severity;

histogram;

**run**;







**proc** **glimmix** data=schizo method=RMPL;

class ID Group (ref="0");

model r\_severity = Group sqrtweek Group\*sqrtweek/solution link=cumlogit dist=multinomial;

random intercept/subject=ID type=UN G;

**run**;

| **Model Information** | |
| --- | --- |
| **Data Set** | WORK.SCHIZO |
| **Response Variable** | r\_severity |
| **Response Distribution** | Multinomial (ordered) |
| **Link Function** | Cumulative Logit |
| **Variance Function** | Default |
| **Variance Matrix Blocked By** | ID |
| **Estimation Technique** | Residual MPL |
| **Degrees of Freedom Method** | Containment |

| **Class Level Information** | | |
| --- | --- | --- |
| **Class** | **Levels** | **Values** |
| **ID** | 413 | 1103 1104 1105 ………..9316 |
| **Group** | 2 | 1 0 |

|  |  |
| --- | --- |
| **Number of Observations Read** | 1652 |
| **Number of Observations Used** | 1500 |

| **Response Profile** | | |
| --- | --- | --- |
| **Ordered Value** | **r\_severity** | **Total Frequency** |
| **1** | 1 | 47 |
| **2** | 2 | 120 |
| **3** | 3 | 166 |
| **4** | 4 | 268 |
| **5** | 5 | 394 |
| **6** | 6 | 421 |
| **7** | 7 | 84 |
| **The GLIMMIX procedure is modeling the probabilities of levels of r\_severity having lower Ordered Values in the Response Profile table.** | | |

| **Dimensions** | |
| --- | --- |
| **G-side Cov. Parameters** | 1 |
| **Columns in X** | 11 |
| **Columns in Z per Subject** | 1 |
| **Subjects (Blocks in V)** | 413 |
| **Max Obs per Subject** | 4 |

| **Optimization Information** | |
| --- | --- |
| **Optimization Technique** | Dual Quasi-Newton |
| **Parameters in Optimization** | 1 |
| **Lower Boundaries** | 1 |
| **Upper Boundaries** | 0 |
| **Fixed Effects** | Profiled |
| **Starting From** | Data |

| **Iteration History** | | | | | |
| --- | --- | --- | --- | --- | --- |
| **Iteration** | **Restarts** | **Subiterations** | **Objective Function** | **Change** | **Max Gradient** |
| **0** | **0** | **4** | 28161.4378 | 2.00000000 | 0.00019 |
| **1** | **0** | **5** | 31754.375232 | 1.21312762 | 0.001151 |
| **2** | **0** | **3** | 32373.253267 | 0.08405759 | 0.000602 |
| **3** | **0** | **2** | 32383.501727 | 0.00164673 | 7.522E-8 |
| **4** | **0** | **2** | 32383.492634 | 0.00015664 | 1.132E-9 |
| **5** | **0** | **1** | 32383.476423 | 0.00000453 | 4.411E-6 |
| **6** | **0** | **0** | 32383.475503 | 0.00000045 | 5.13E-6 |
| **7** | **0** | **0** | 32383.475457 | 0.00000002 | 5.602E-6 |
| **8** | **0** | **0** | 32383.475454 | 0.00000000 | 5.633E-6 |

|  |
| --- |
| Convergence criterion (PCONV=1.11022E-8) satisfied. |

| **Fit Statistics** | |
| --- | --- |
| **-2 Res Log Pseudo-Likelihood** | 32383.48 |

| **Estimated G Matrix** | | |
| --- | --- | --- |
| **Effect** | **Row** | **Col1** |
| Intercept | **1** | 1.0920 |

| **Covariance Parameter Estimates** | | | |
| --- | --- | --- | --- |
| **Cov Parm** | **Subject** | **Estimate** | **Standard Error** |
| **UN(1,1)** | ID | 1.0920 | 0.1399 |

| **Solutions for Fixed Effects** | | | | | | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Effect** | **r\_severity** | **Group** | **Estimate** | **Standard Error** | **DF** | **t Value** | **Pr > |t|** |
| **Intercept** | 1 |  | -5.3218 | 0.2523 | 411 | -21.09 | <.0001 |
| **Intercept** | 2 |  | -3.8528 | 0.2188 | 411 | -17.61 | <.0001 |
| **Intercept** | 3 |  | -2.8738 | 0.2090 | 411 | -13.75 | <.0001 |
| **Intercept** | 4 |  | -1.7987 | 0.2015 | 411 | -8.93 | <.0001 |
| **Intercept** | 5 |  | -0.4393 | 0.1951 | 411 | -2.25 | 0.0249 |
| **Intercept** | 6 |  | 1.9550 | 0.2127 | 411 | 9.19 | <.0001 |
| **Group** |  | 1 | -0.01599 | 0.2220 | 1080 | -0.07 | 0.9426 |
| **Group** |  | 0 | 0 | . | . | . | . |
| **sqrtweek** |  |  | 0.4862 | 0.1138 | 1080 | 4.27 | <.0001 |
| **sqrtweek\*Group** |  | 1 | 0.8172 | 0.1299 | 1080 | 6.29 | <.0001 |
| **sqrtweek\*Group** |  | 0 | 0 | . | . | . | . |

| **Type III Tests of Fixed Effects** | | | | |
| --- | --- | --- | --- | --- |
| **Effect** | **Num DF** | **Den DF** | **F Value** | **Pr > F** |
| **Group** | 1 | 1080 | 0.01 | 0.9426 |
| **sqrtweek** | 1 | 1080 | 176.53 | <.0001 |
| **sqrtweek\*Group** | 1 | 1080 | 39.60 | <.0001 |