An ordinal regression model with random intercept

Contents

1. Introduction

An ordinal variable is a categorical variable where there is a logical ordering to the categories. In most cases, treating an ordinal outcome as a continuous variable is inadvisable. As in the case of a binary outcome variable, a link function is used in order to take the ceiling and floor effects of the ordinal outcome into account. The available link functions in LISREL include probit, logistic, complementary log-log and log-log.

2. The model

Let the outcome variable be coded into c categories, where $c = 1, 2, ..., C$. In this example, the ordinal variable IMPS79O defines the severity of the illness in terms of four categories, and thus $C = 4$. As ordinal models utilize cumulative comparisons of the categories, define the cumulative probabilities for the C categories of the outcome Y as $P_{ijc} = \Pr\left(Y_{ij} \le c\right) = \sum_{k=1}^{c} p_{ijk}$, where p_{ijk} represents the probability that the response of the j-th measurement on patient i occurs in category k.

The type of drug, time elapsed since start of treatment, and the interaction between drug taken and time elapsed are of interest as predictors. The logistic regression model with IMPS79O as outcome can then be written as

Level-1 model:

$$y_{ij} = \log\left(\frac{P_{ijc}}{1-P_{ijc}}\right) = \gamma_c - \left[b_{0i} + b_{1i}\text{DRUG}_i + b_{2i}\text{SQRTWEEK}_i + b_{3i}\left(\text{WSQRT}\times\text{DR}\right)_i\right],$$
$$j = 1,\ldots,n_i;\ c = 1,2,\ldots,C-1$$

Level-2 model:

$$b_{0i} = \beta_0 + v_{0i},\quad i = 1,\ldots,N$$
$$b_{1i} = \beta_1$$
$$b_{2i} = \beta_2$$
$$b_{3i} = \beta_3$$

The cumulative probability can be expressed by

$$P_{ijc} = \frac{e^{\gamma_c - \left[b_{0i} + b_{1i}\text{DRUG}_i + b_{2i}\text{SQRTWEEK}_i + b_{3i}\left(\text{WSQRT}\times\text{DR}\right)_i\right]}}{1 + e^{\gamma_c - \left[b_{0i} + b_{1i}\text{DRUG}_i + b_{2i}\text{SQRTWEEK}_i + b_{3i}\left(\text{WSQRT}\times\text{DR}\right)_i\right]}}$$

To obtain the probability for category c ,

$$p_{ij,c} = P_{ij,c+1} - P_{ij,c}$$

As shown above, the intercept b_{0i} is estimated by a level-2 equation. It indicates that patient *i*'s initial IMPS79O value is not only determined by the population average β_0 , but also by the patient difference v_{0i} . In other words, patients may have different average intercepts, and the model makes provision for this eventuality. The slopes are assumed to be the same for all the patients, which imply that each patient's trend line is parallel to the population trend.

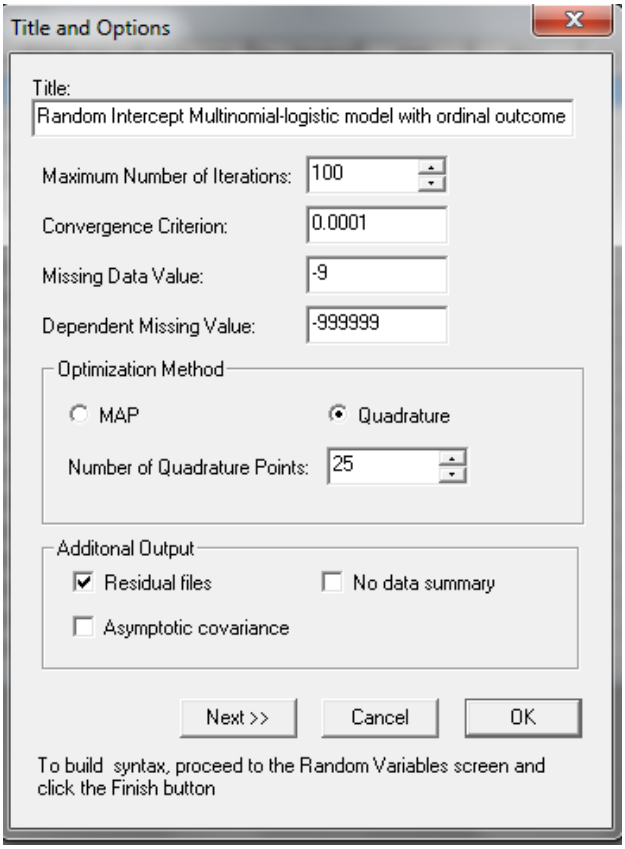
The connection between an ordinal outcome variable y with C categories and an underlying continuous variable y^* is

$$y = c \leftrightarrow \gamma_{j-1} \le y^* \le \gamma_j,\ c = 1,2,...,C$$

where it is assumed that $\gamma_0 = -\infty$ and $\gamma_C = +\infty$. In addition, γ_1 is usually set to 0 to avoid identification problems.

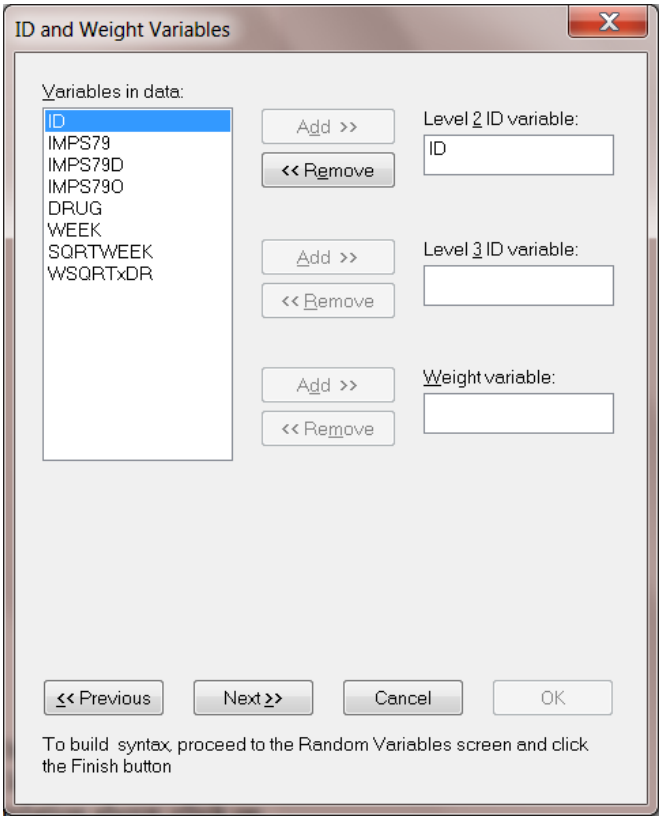
3. Setting up the analysis

Open the LISREL spreadsheet **nimh_study.lsf** and select **Title and Options** option on the **Multilevel, Generalized Linear Model** menu.

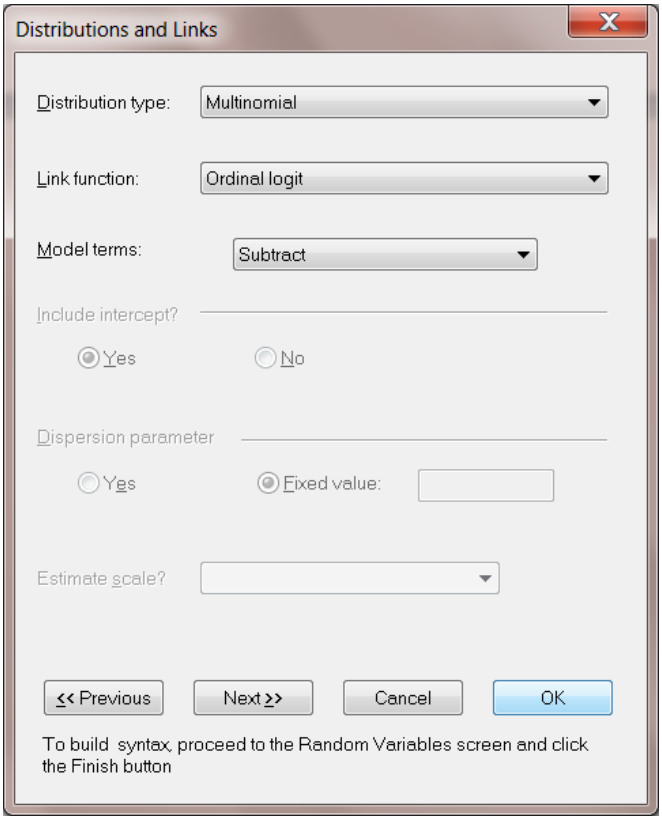


In the **Title and Options** dialog box, enter a title for the analysis in the **Title** text boxes. Keep the default settings for the **Maximum Number of Iterations** and **Convergence Criterion**. The **Missing Data Value** text box is used to specify the values of missing data for both outcome and predictors. We notice that the missing value –9 is presented in the data. Define the missing value by entering the number -9 in the **Missing Data Value** text box as shown above. Activate **Quadrature** radio button in the **Optimization Method** section and change the **Number of Quadrature Points** to 25 to obtain the above screen. Proceed to the **ID and Weight Variables** dialog box by clicking on the **Next** button.

Select ID from the **Variables in data** list box. Click on the **Add** button of the **Level-2 ID variable** section to obtain the following dialog box.

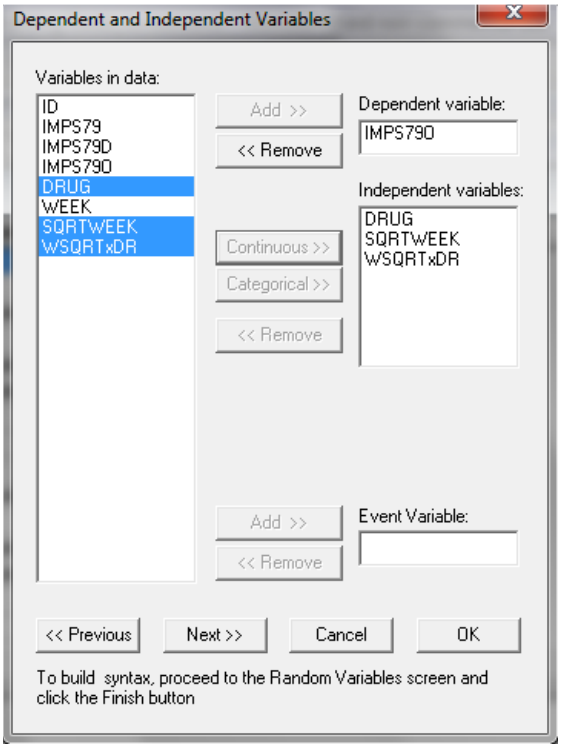


Proceed to the **Distribution and Links** dialog box by clicking on the **Next** button. Use the default **Distribution type**, which is **Multinomial**. The default link function is the logit link function. To change it to the ordinal logit link function corresponding to the model formulation above, click on the **Link function** drop-down list and select the **Ordinal logit** link function. Select **Subtract** from the **Model terms** drop-down list box as shown below.

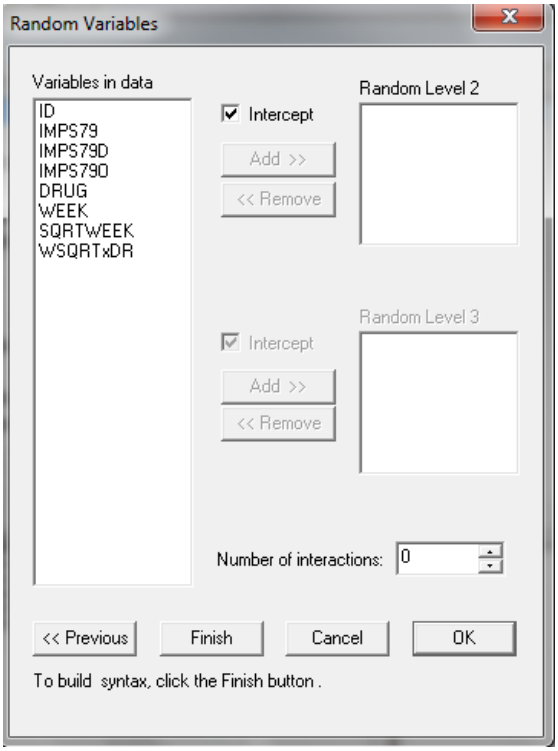


Click on the **Next** button to proceed to the **Dependent and Independent Variables** dialog box.

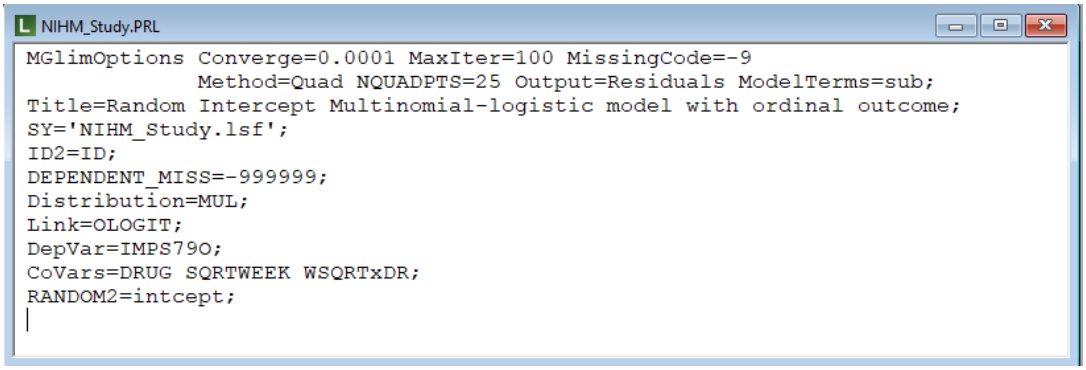
The **Dependent and Independent Variables** dialog box is used to specify the dependent and independent variables. First, select the dependent variable IMPS79O from the **Variables in data** list box and then click on the **Add** button to define it as the **Dependent variable**. Next, select DRUG, SQRTWEEK and WSQRTxDR one at a time and click on the **Continuous** button to add them as **Independent variables** as shown below.



Click on the **Next** button to activate the Random Variables dialog box. By default, the **Intercept** check box in the **Random Level-2** is checked, indicating the inclusion of a random intercept at this level in the model. Keep the default settings as shown below and click on the **Finish** button to generate the PRELIS syntax (**prl**) file.



Before running the analysis, the PRELIS syntax file could be saved under a different file name. Select the **File**, **Save As** option, and provide a name (**nimh_study1.prl**) for the syntax file. Run the analysis by selecting the **Run PRELIS** icon as shown below.



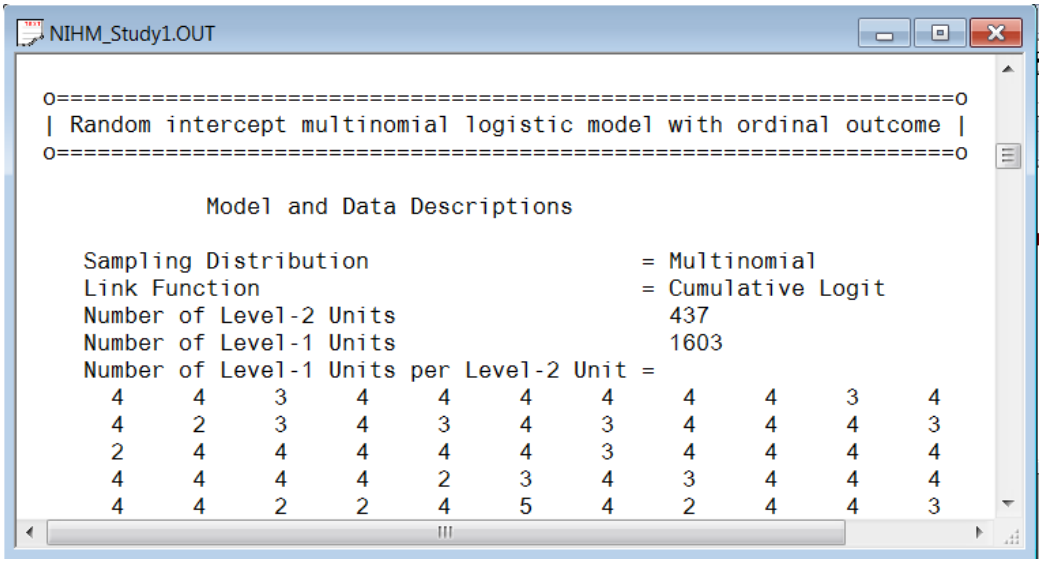
4. Discussion of results

Syntax

The syntax lines are repeated in the output file corresponding to the PRELIS syntax (***.prl**) file we saved.

Model and data description

The next section of the output file contains a description of the hierarchical structure and model specifications. The use of a logistic response function (logit link function) with the assumption of a normal distribution of random effects is indicated. This is followed by a summary of the number of observations nested within each patient. As shown below, 437 patients with a total of 1603 observations are included in this study after listwise deletion. The number of observations per patient (level-2 unit) varies between 2 and 5.



Descriptive statistics and starting values

Next, the descriptive statistics for all the variables are given. Notice that the variable name WSQRTxDR is truncated to WSQRTxDR. This is because LISREL only recognizes the first 8 characters of a variable name.

NIHM_Study1.OUT

| Descriptive statistics for all the variables in the model |

Variable	Minimum	Maximum	Mean	Standard Deviation
IMPS7901	0.0000	1.0000	0.1185	0.3233
IMPS7902	0.0000	1.0000	0.2957	0.4565
IMPS7903	0.0000	1.0000	0.2570	0.4371
IMPS7904	0.0000	1.0000	0.3288	0.4699
DRUG	0.0000	1.0000	0.7642	0.4246
SQRTWEEK	0.0000	2.4495	1.2204	0.8965
WSQRTxDR	0.0000	2.4495	0.9442	0.9454

Descriptive statistics are followed by the parameter estimates of a model with no random effects.

NIHM_Study.OUT

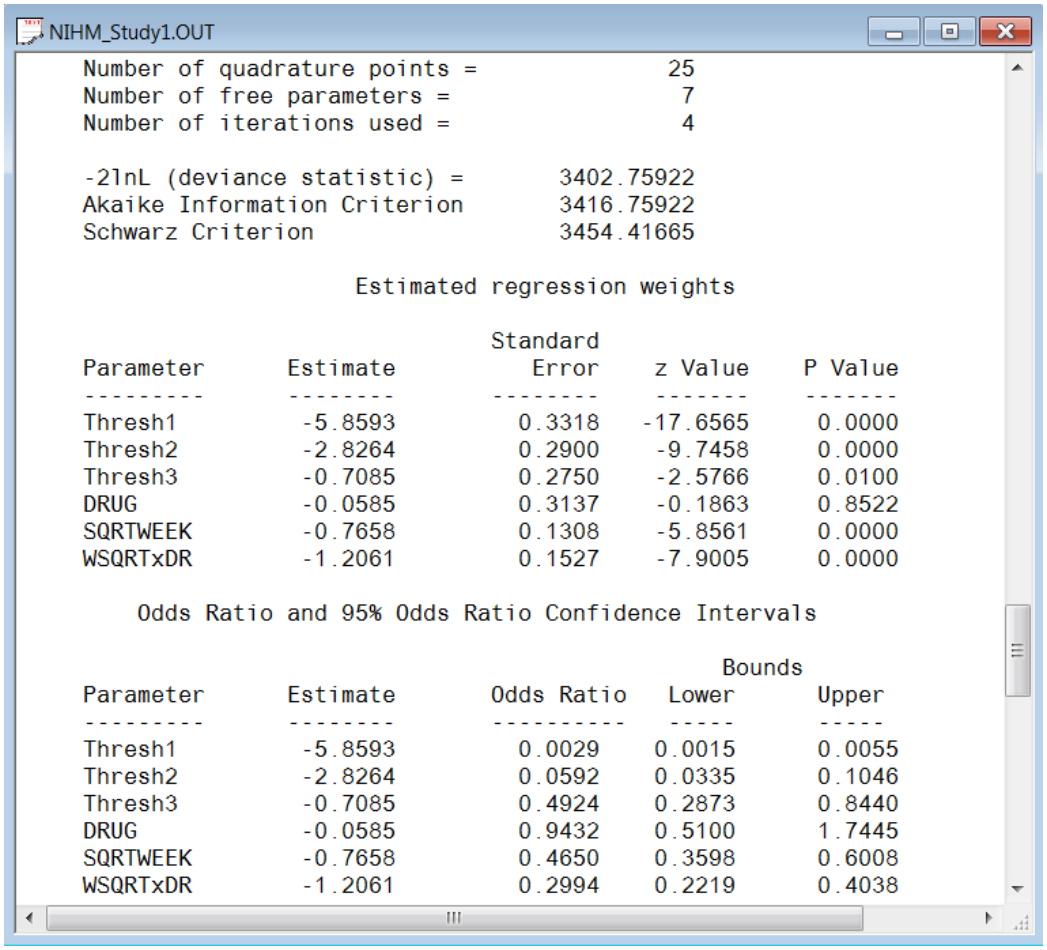
Goodness of fit statistics

Statistic	Value	DF	Ratio
Likelihood Ratio Chi-square	3756.1953	1597	2.3520
Pearson Chi-square	4426.5403	1597	2.7718
Log Likelihood	-1878.0976		
Akaike Information Criterion	3768.1953		
Schwarz Criterion	3800.4731		

Estimated regression weights

Parameter	Estimate	Standard Error	z Value	P Value
Thresh1	-3.8073	0.1899	-20.0532	0.0000
Thresh2	-1.7602	0.1703	-10.3375	0.0000
Thresh3	-0.4221	0.1636	-2.5796	0.0099
DRUG	-0.0006	0.1883	-0.0032	0.9974
SQRTWEEK	-0.5366	0.1108	-4.8427	0.0000
WSQRTxDR	-0.7510	0.1277	-5.8817	0.0000

The final results after 4 iterations are shown next. The estimates are shown in the column with heading Estimate and correspond to the coefficients $\beta_0, \beta_1, \ldots, \beta_3$ in the model specification. The standard error, *z*-value and *p*-value are also printed.

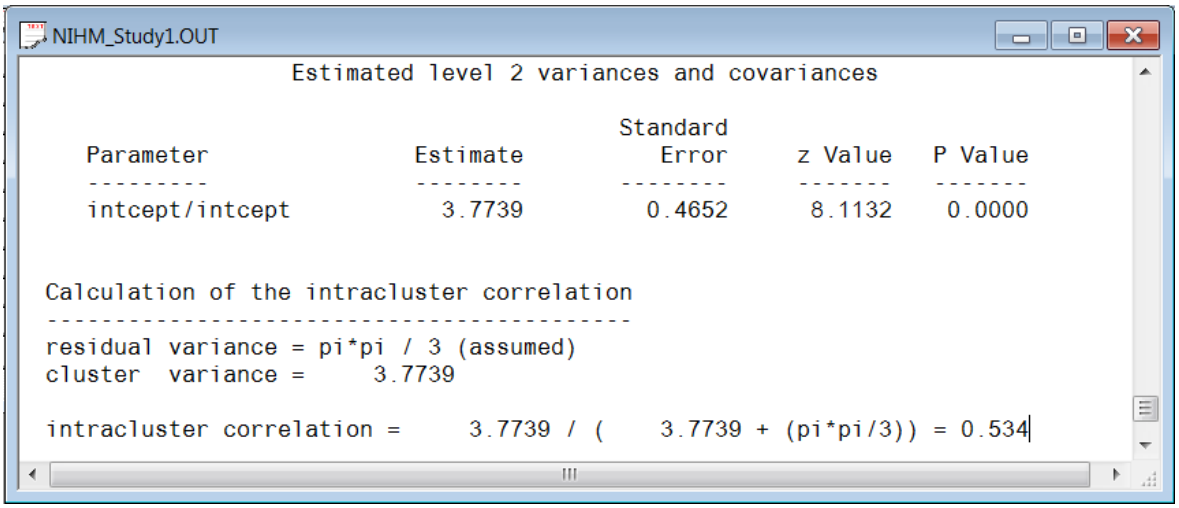


The variation in the intercept over the subjects is estimated as 3.7739, and from the associated *p*-value we conclude that there is significant variation in the (random) intercept between the patients included in this analysis. In the case of the fixed effects, a 2-tailed *p*-value is used, as the alternative hypothesis considered here is of the form $H_1 : \beta \neq 0$. As variances are constrained to be elements of the interval $[0, +\infty)$ and thresholds are constrained so that $\gamma_1 \leq \gamma_2 \leq \gamma_3$, the *p*-values used for these effects are 1-tailed. The results indicate that the treatment groups do not differ significantly at baseline (the estimated DRUG coefficient is not significant). The placebo group seems to improve over time, as the SQRTWEEK coefficient is both significant and negative. Note that the interpretation of the main effects depends on the coding of the variable, and on the significance of the WSQRTxDR interaction which forms part of the model.

As noted before, it is assumed that $\gamma_0 = -\infty$ and $\gamma_C = +\infty$. For the present example, C = 4, and from the output we see that $\hat{\gamma}_1 = -5.8593$, $\hat{\gamma}_2 = -2.8264$ and $\hat{\gamma}_3 = -0.7085$. These values are used in combination with the coefficients of DRUG, SQRTWEEK, and WSQRTxDR to calculate estimated outcomes for different groups of patients.

Intraclass correlation (ICC)

An estimate of the level-2 variance of the intercept and of the intracluster correlation (ICC) is given in the next section of the output. The residual variance for the logistic link function is assumed to be $\pi^2/3$.



The ICC in this model refers to the intra-person correlation. It is reported as 0.534, which is fairly high. Generally, the shorter the interval between the repeated measurements, the higher the ICCs will be.

5. Interpreting the output

Estimated outcomes for groups: unit-specific probabilities

To evaluate the expected effect of the treatment group and the square root of time of treatment, while allowing for the interaction between treatment and the square of time, we use the expression below:

$$\log\left(\frac{\hat{P}_{ijc}}{1-\hat{P}_{ijc}}\right) = \hat{\gamma}_c - \left[\,\hat{b}_{1i}\mathrm{DRUG}_i + \hat{b}_{2i}\mathrm{SQRTWEEK}_i + \hat{b}_{3i}\left(\mathrm{WSQRT}\times\mathrm{DRUG}\right)_i\,\right]$$

or, in the notation introduced in Section 2,

$$\log\left(\frac{\hat{P}_{ijc}}{1-\hat{P}_{ijc}}\right) = \hat{\eta}_{ijc}$$
$$= \hat{\gamma}_c - 0.0585\times\mathrm{DRUG}_i + 0.7658\times\mathrm{SQRTWEEK}_i$$
$$+1.2061\times\left(\mathrm{WSQRT}\times\mathrm{DRUG}\right)_i.$$

When c = 1, we find that, for a patient from the control group (DRUG = 0, SQRTWEEK = WSQRTxDR = 0),

$$\log\left(\frac{\hat{P}_{ij1}}{1-\hat{P}_{ij1}}\right)=\hat{\eta}_{ij1}=-5.8593$$

$$\hat{P}_{ij1}=\frac{e^{\hat{\eta}_{ij1}}}{1+e^{\hat{\eta}_{ij1}}}=0.0028$$

Similarly, the probabilities that a typical patient from the control group responded in a specific category at the start of the study are obtained by using $\hat{\gamma}_2=-2.8264$, and $\hat{\gamma}_3=-0.7085$.

The cumulative probabilities we calculated are

$$\hat{P}_{ij2}=\frac{e^{\hat{\eta}_{ij2}}}{1+e^{\hat{\eta}_{ij2}}}=\frac{e^{-2.8264}}{1+e^{-2.8264}}=0.0559$$

$$\hat{P}_{ij3}=\frac{e^{\hat{\eta}_{ij3}}}{1+e^{\hat{\eta}_{ij3}}}=\frac{e^{-0.7085}}{1+e^{-0.7085}}=0.3299.$$

Thus, the estimated category probabilities we have for such a group (category 1 to 4) are obtained as

$$\hat{p}_{ij1}=0.0028-0=0.0028$$
$$\hat{p}_{ij2}=0.0559-0.0028=0.0531$$
$$\hat{p}_{ij3}=0.3299-0.059=0.2740$$
$$\hat{p}_{ij4}=1-0.3299=0.6701.$$

For this group of patients (DRUG = 0) at the starting week, the expected percentages of patients in each of the categories are as follows: 0.3% of the patients are normal or borderline mentally ill; 5.3% of the patients are mildly or moderately ill; 27.4% are markedly ill and 67% are severely or extremely ill. Similarly, we can calculate the estimated percentages for both groups at all the time points as shown in Table 8.

The contents of Table 8 can be graphically represented as shown in Figures 3 and 4. It clearly shows that the numbers of markedly and severely ill patients decrease dramatically over time. The improvement for the drug patients is larger than the placebo patients.

Table 6: Estimated % for both groups at 7 time points

	Drug patients (drug = 1)				Placebo patients (drug = 0)			
severity	normal	moderate	marked	severe	normal	moderate	marked	severe
week 0	0.30%	5.61%	28.39%	65.70%	0.28%	5.31%	27.40%	67.01%
week 1	0.65%	11.25%	40.99%	47.11%	2.01%	27.84%	48.11%	22.04%
week 2	0.89%	14.76%	45.02%	39.34%	4.43%	44.62%	39.84%	11.10%
week 3	1.13%	18.00%	47.16%	33.71%	7.99%	56.32%	29.43%	6.26%
week 4	1.38%	21.13%	48.21%	29.28%	12.84%	62.51%	20.87%	3.79%
week 5	1.65%	24.17%	48.50%	25.69%	19.00%	63.96%	14.63%	2.41%
week 6	1.94%	27.13%	48.24%	22.69%	26.32%	61.79%	10.29%	1.60%

6. A 2-level random intercept model and trend model

In this section, we fit a model with random intercept and slope. To do this, the level-1 model is unchanged; only the level-2 model is modified.

7. The model

Level-1 model:

$$y_{ij} = \log\left(\frac{P_{ijc}}{1-P_{ijc}}\right) = \gamma_c - \left[b_{0i} + b_{1i}\text{DRUG}_i + b_{2i}\text{SQRTWEEK}_i + b_{3i}\left(\text{WSQRT}\times\text{DRUG}\right)_i\right],$$
$$j = 1,\ldots,n_i;\ c = 1,2,\ldots,C-1$$

Level-2 model:

$$b_{0i} = \beta_0 + v_{0i}, \quad i = 1,\ldots,N$$
$$b_{1i} = \beta_1$$
$$b_{2i} = \beta_2 + v_{2i}$$
$$b_{3i} = \beta_3$$

As shown above, the slope of the time variable b_{2i} is now estimated by a level-2 equation containing both a fixed and a random effect. It indicates that patients are now not only assumed to have different intercepts, but may also exhibit different responses to the treatment over time.

8. Setting up the analysis

In this example, we want to use 10 quadrature points and include SQRTWEEK as level-2 random effect. We modify the commands syntax previously saved to **nimh_study1.prl** to obtain the new model setup.

First, click on **File**, **Open** to browse and open **nimh_study1.prl**. Next, we change the string in the **NQUADPTS = 10** in the MGLIM command. Change **RANDOM2 = intcept SQRTWEEK** and save the syntax file to **nimh_study2.prl**.

```
MGlimOptions Converge=0.0001 MaxIter=100 MissingCode=-9
             Method=Quad NQUADPTS=25 Output=Residuals ModelTerms=sub;
Title=Random Intercept Multinomial-logistic model with ordinal outcome;
SY='NIHM_Study.lsf';
ID2=ID;
DEPENDENT_MISS=-999999;
Distribution=MUL;
Link=OLOGIT;
DepVar=IMPS79O;
CoVars=DRUG SQRTWEEK WSQRTxDR;
RANDOM2=intcept SQRTWEEK;
```

Click on the **Run PRELIS** icon to produce the output file **nimh_study2.out**.

NIHM_Study2.OUT

```
o================================================o
| Results for the model without any random effects |
o================================================o

                    Goodness of fit statistics

   Statistic                                 Value          DF          Ratio
   ---------                                 -----          --          -----
   Likelihood Ratio Chi-square            3756.1953        1597         2.3520
   Pearson Chi-square                     4426.5410        1597         2.7718

                    Estimated regression weights

                              Standard
   Parameter      Estimate       Error    z Value    P Value
   ---------      --------     --------    -------    -------
   Thresh1         -3.8073       0.1899   -20.0532     0.0000
   Thresh2         -1.7602       0.1703   -10.3375     0.0000
   Thresh3         -0.4221       0.1636    -2.5796     0.0099
   DRUG            -0.0006       0.1883    -0.0032     0.9974
   SQRTWEEK        -0.5366       0.1108    -4.8427     0.0000
   WSQRTxDR        -0.7510       0.1277    -5.8817     0.0000

       Odds Ratio and 95% Odds Ratio Confidence Intervals

                                                 Bounds
   Parameter      Estimate      Odds Ratio    Lower      Upper
   ---------      --------      ----------    -----      -----
   Thresh1         -3.8073        0.0222     0.0153     0.0322
   Thresh2         -1.7602        0.1720     0.1232     0.2402
   Thresh3         -0.4221        0.6557     0.4758     0.9036
   DRUG            -0.0006        0.9994     0.6909     1.4456
   SQRTWEEK        -0.5366        0.5847     0.4706     0.7266
   WSQRTxDR        -0.7510        0.4719     0.3674     0.6061
```

9. Discussion of results

Fixed effect results, adaptive quadrature

The final results after 7 iterations are listed below. While the values of the estimated coefficients differ from those in the random-intercept-only model, the overall picture remains very similar. The decline in severity over time noticed in the crosstabulation is captured by the significant fixed effect coefficient of –0.8840 for SQRTWEEK.

NIHM_Study2.OUT

```
o=========================================o
| Optimization Method: Adaptive Quadrature |
o=========================================o

   Number of quadrature points =              10
   Number of free parameters =                 9
   Number of iterations used =                 7

   -2lnL (deviance statistic) =       3325.49276
   Akaike Information Criterion       3343.49276
   Schwarz Criterion                  3391.90945


                    Estimated regression weights

                                 Standard
   Parameter      Estimate          Error    z Value    P Value
   ---------      --------       --------    -------    -------
   Thresh1         -7.3234         0.4726   -15.4954     0.0000
   Thresh2         -3.4214         0.3862    -8.8597     0.0000
   Thresh3         -0.8151         0.3517    -2.3177     0.0205
   DRUG             0.0553         0.3912     0.1414     0.8875
   SQRTWEEK        -0.8840         0.2183    -4.0495     0.0001
   WSQRTxDR        -1.6939         0.2525    -6.7091     0.0000
```

Random effects results

Note that the estimated coefficient for the random SQRTWEEK slope is highly significant, indicating that patients not only start at different points but follow different paths during the treatment period.

NIHM_Study2.OUT

```
                Estimated level 2 variances and covariances

                                        Standard
   Parameter              Estimate          Error    z Value    P Value
   ---------              --------       --------    -------    -------
   intcept/intcept          7.0058         1.3190     5.3114     0.0000
   SQRTWEEK/intcept        -1.5122         0.5320    -2.8424     0.0045
   SQRTWEEK/SQRTWEEK        2.0118         0.4181     4.8112     0.0000
```

10. Interpreting the output

Estimated outcomes for groups: unit-specific results

To evaluate the expected effect of the treatment group and the square root of time of treatment, while allowing for the interaction between treatment and the square root of time, we use the expression below:

$$\log\left(\frac{\hat{P}_{ijc}}{1-\hat{P}_{ijc}}\right)=\hat{\gamma}_c-\left[\hat{b}_{0i}+\hat{b}_{1i}\text{DRUG}_i+\hat{b}_{2i}\text{SQRTWEEK}_i+\hat{b}_{3i}\left(\text{WSQRT}\times\text{DRUG}\right)_i\right]$$

so that

$$\hat{\eta}_{ijc}=\hat{\gamma}_c-7.3793+0.0553\times\text{DRUG}_i+0.8841\times\text{SQRTWEEK}_i$$
$$+1.6940\times\left(\text{WSQRT}\times\text{DRUG}\right)_i$$

As illustrated in the previous example, by substituting the values for DRUG, SQRTWEEK and WSQRTxDR, the results shown in Table 7 can be obtained.

Table 7: Estimated unit-specific results for random intercept & slope model

	Placebo patients (drug = 0)				Drug patients (drug = 1)			
severity	normal	moderate	marked	severe	normal	moderate	marked	severe
week 0	0.06%	2.96%	26.90%	70.08%	0.07%	3.13%	27.90%	68.91%
week 1	0.15%	6.87%	43.81%	49.17%	0.86%	29.42%	55.32%	14.40%
week 2	0.22%	9.61%	50.03%	40.15%	2.47%	51.90%	39.98%	5.81%
week 3	0.29%	12.32%	53.77%	33.62%	5.42%	68.72%	23.37%	2.49%
week 4	0.36%	15.09%	55.99%	28.55%	10.27%	74.85%	13.62%	1.26%
week 5	0.45%	17.94%	57.12%	24.49%	17.38%	73.94%	7.99%	0.69%
week 6	0.54%	20.84%	57.44%	21.17%	26.72%	68.08%	4.80%	0.40%

We can again represent the results from the above table graphically, as shown in Figures 5 and 6. The graphs tell us the same story as the previous model: patients from the treatment group showed more improvement over time than patients from the control group. While a very small proportion of treatment patients were still diagnosed as being severely ill at the end of the treatment period (0.42% according to table 9), 20% of the control group were still classified as being severely ill by week 6.

Estimated time trend variance

When we consider the heterogeneity in responses across time, we notice that the estimated variance in the time trend is $\sigma^2_{v_1}=(1.29774)^2+(-0.57054)^2=2.0096$. The estimates for the time trends are -0.88295 for SQRTWEEK and -1.69416 for WSQRTxDR respectively. Thus the estimated trends for the placebo and drug groups are -0.88295 and -0.88295 -1.69416 = -2.57711. Thus the 95% confidence interval of the time trend for the placebo group is $-0.88295\pm\left(1.96\times\sqrt{2.0096}\right)$ $=(-3.6615,1.896)$. Similarly, the confidence interval for the drug group is $(-5.3556, 0.2014)$. Notice that both intervals are fairly large and include negative and positive slopes, which reflects

the wide heterogeneity in trends. The estimated correlation value is –0.402, which is moderately large. This indicates that the patients who are initially less severely ill improve at a smaller rate. The more severely ill patients improve at a greater rate.