Mixed Models for Longitudinal Binary Outcomes

Don Hedeker
Department of Public Health Sciences
Biological Sciences Division
University of Chicago

hedeker@uchicago.edu

Hedeker, D. (2005). Generalized linear mixed models. In B. Everitt & D. Howell (Eds.), Encyclopedia of Statistics in Behavioral Science. Wiley.

Hedeker, D. & Gibbons, R.D. (2006). Longitudinal Data Analysis, chapter 9. Wiley.

This work was supported by National Institute of Mental Health Contract N44MH32056.

Mixed-effects models for categorical outcomes

- dichotomous outcomes
  - mixed-effects logistic regression

- ordinal outcomes
  - mixed-effects ordinal logistic regression
    - proportional odds model
    - partial or non-proportional odds model

- nominal outcomes
  - mixed-effects nominal logistic regression

- discrete or grouped time-to-event data
  - mixed-effects dichotomous or ordinal regression
    - complementary log-log link for proportional (and non-proportional) hazards models

Logistic Regression Model

$$\log\left[\frac{P(Y_i = 1)}{1 - P(Y_i = 1)}\right] = \boldsymbol{x}_i'\boldsymbol{\beta}$$

- Dichotomous outcome ($Y = 0$ absence, $Y = 1$ presence).
- Function that links probabilities to regressors is the logit (or log odds) function $\log\left[P/(1-P\right]$. Logit is called the link function.

The model can be written in terms of probabilities:

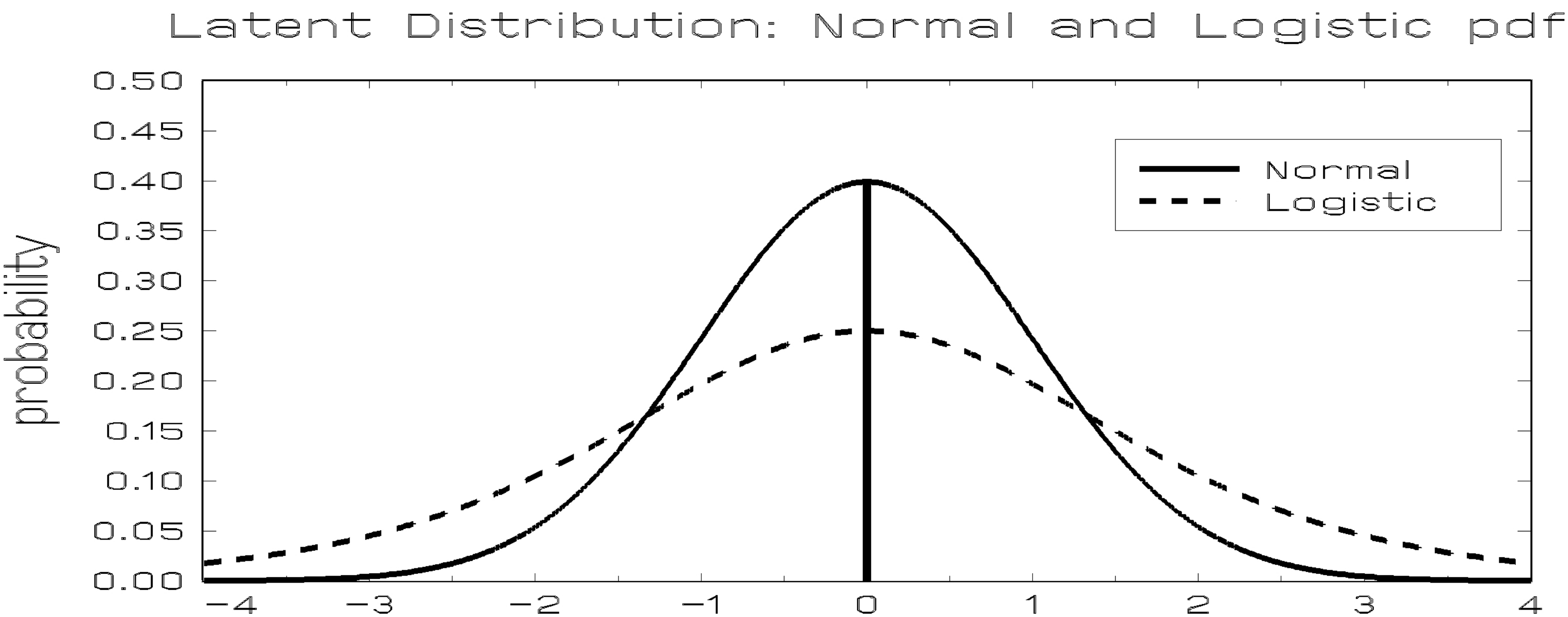
$$P(Y_i = 1) = \frac{1}{1 + \exp(-\boldsymbol{x}_i'\boldsymbol{\beta})}$$

- Model is a linear model for the logits, not for the probabilities. Logits can take on any values between negative and positive infinity, probabilities can only take on values between 0 and 1

Dichotomous Response and Threshold Concept

Continuous y_i - an unobservable latent variable - related to dichotomous response Y_i via "threshold concept"

Response occurs ($Y_i = 1$) if $\gamma < y_i$
otherwise, a response does not occur ($Y_i = 0$)



The Threshold Concept in Practice

"How was your day?" (what is your satisfaction level today?)

- Satisfaction may be continuous, but we usually emit a dichotomous response:

Model for Latent Continuous Responses

Consider the model with p covariates for the latent response strength y_i ($i = 1, 2, \ldots, N$):

$$y_i = \boldsymbol{x}_i'\boldsymbol{\beta} + \varepsilon_i$$

- probit: $\varepsilon_i \sim$ standard normal (mean=0, variance=1)
- logistic: $\varepsilon_i \sim$ standard logistic (mean=0, variance=$\pi^2/3$)

$\Rightarrow \boldsymbol{\beta}$ estimates from logistic regression are larger (in abs. value) than from probit regression by approximately $\sqrt{\pi^2/3} = 1.8$

Underlying latent variable

- useful way of thinking of the problem
- not an essential assumption of the model

Random-intercept Logistic Regression Model

Consider the model with p covariates for the response Y_{ij} for subject i ($i = 1, 2, \ldots, N$) at time j ($j = 1, 2, \ldots, n_i$):

$$\log \left[\frac{P(Y_{ij} = 1 \mid \upsilon_{0i})}{1 - P(Y_{ij} = 1 \mid \upsilon_{0i})} \right] = \boldsymbol{x}'_{ij} \boldsymbol{\beta} + \upsilon_{0i}$$

where

$$\begin{aligned} Y_{ij} &= \text{dichotomous response for subject } i \text{ at time } j \\ \boldsymbol{x}_{ij} &= (p+1) \times 1 \text{ covariate vector (includes 1 for intercept)} \\ \boldsymbol{\beta} &= (p+1) \times 1 \text{ vector of unknown parameters} \\ \upsilon_{0i} &= \text{subject effects distributed } \mathcal{NID}(0, \sigma_\upsilon^2) \end{aligned}$$

Model for Latent Continuous Responses

Consider the model with p covariates for the $n_i \times 1$ latent response strength y_{ij}:

$$y_{ij} = \boldsymbol{x}'_{ij}\boldsymbol{\beta} + \upsilon_{0i} + \varepsilon_{ij}$$

where assuming

- $\varepsilon_{ij} \sim$ standard normal (mean 0 and $\sigma^2 = 1$) leads to mixed-effects probit regression
- $\varepsilon_{ij} \sim$ standard logistic (mean 0 and $\sigma^2 = \pi^2/3$) leads to mixed-effects logistic regression

Underlying latent variable

- not an essential assumption of the model
- useful for obtaining intra-class correlation (r)

$$r = \frac{\sigma_v^2}{\sigma_v^2 + \sigma^2}$$

and for design effect (d)

$$d = \frac{\sigma_v^2 + \sigma^2}{\sigma^2} = 1/(1 - r)$$

ratio of actual variance to the variance that would be obtained by simple random sampling (holding sample size constant)

Scaling of regression coefficients

$\boldsymbol{\beta}$ estimates from mixed-effects model are larger (in abs. value) than from fixed-effects model by approximately

$$\sqrt{d} = \sqrt{\frac{\sigma_\upsilon^2 + \sigma^2}{\sigma^2}}$$

because

- $V(y) = \sigma_\upsilon^2 + \sigma^2$ in mixed-effects model
- $V(y) = \sigma^2$ in fixed-effects model

difference depends on size of random-effects variance σ_υ^2

Treatment-Related Change Across Time

Data from the NIMH Schizophrenia collaborative study on treatment related changes in overall severity. IMPS item 79, *Severity of Illness*, was scored as:

1	=	normal
2	=	borderline mentally ill
3	=	mildly ill
4	=	moderately ill
5	=	markedly ill
6	=	severely ill
7	=	among the most extremely ill

The experimental design and corresponding sample sizes:

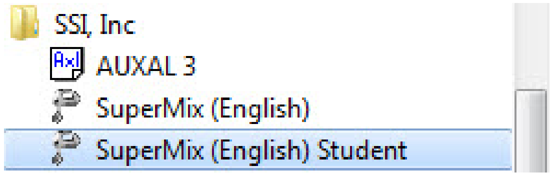
	Sample size at Week							
Group	0	1	2	3	4	5	6	*completers*
PLC (n=108)	107	105	5	87	2	2	70	65%
DRUG (n=329)	327	321	9	287	9	7	265	81%

Drug = Chlorpromazine, Fluphenazine, or Thioridazine

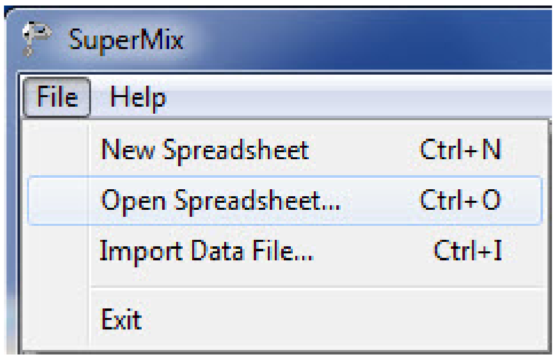
Main question of interest:

- Was there differential improvement for the drug groups relative to the control group?

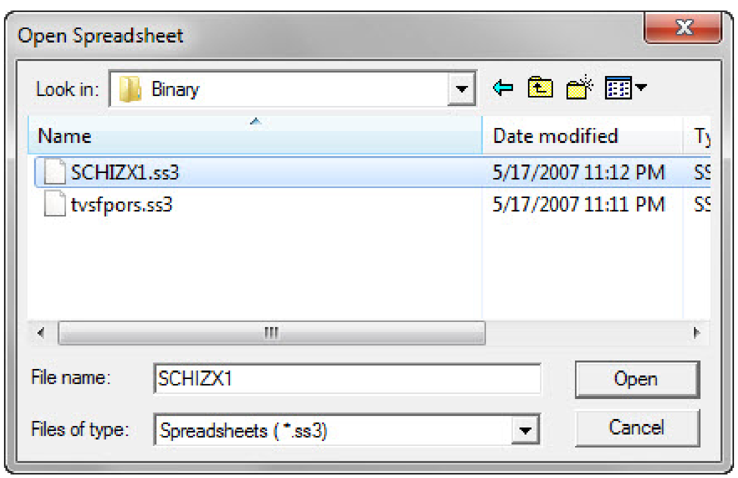
- Under SSI, Inc > "SuperMix (English)" or "SuperMix (English) Student"



- Under "File" click on "Open Spreadsheet"



- Open C:\SuperMixEn Examples\Workshop\Binary\SCHIZX1.ss3
  (or C:\SuperMixEn Student Examples\Workshop\Binary\SCHIZX1.ss3)



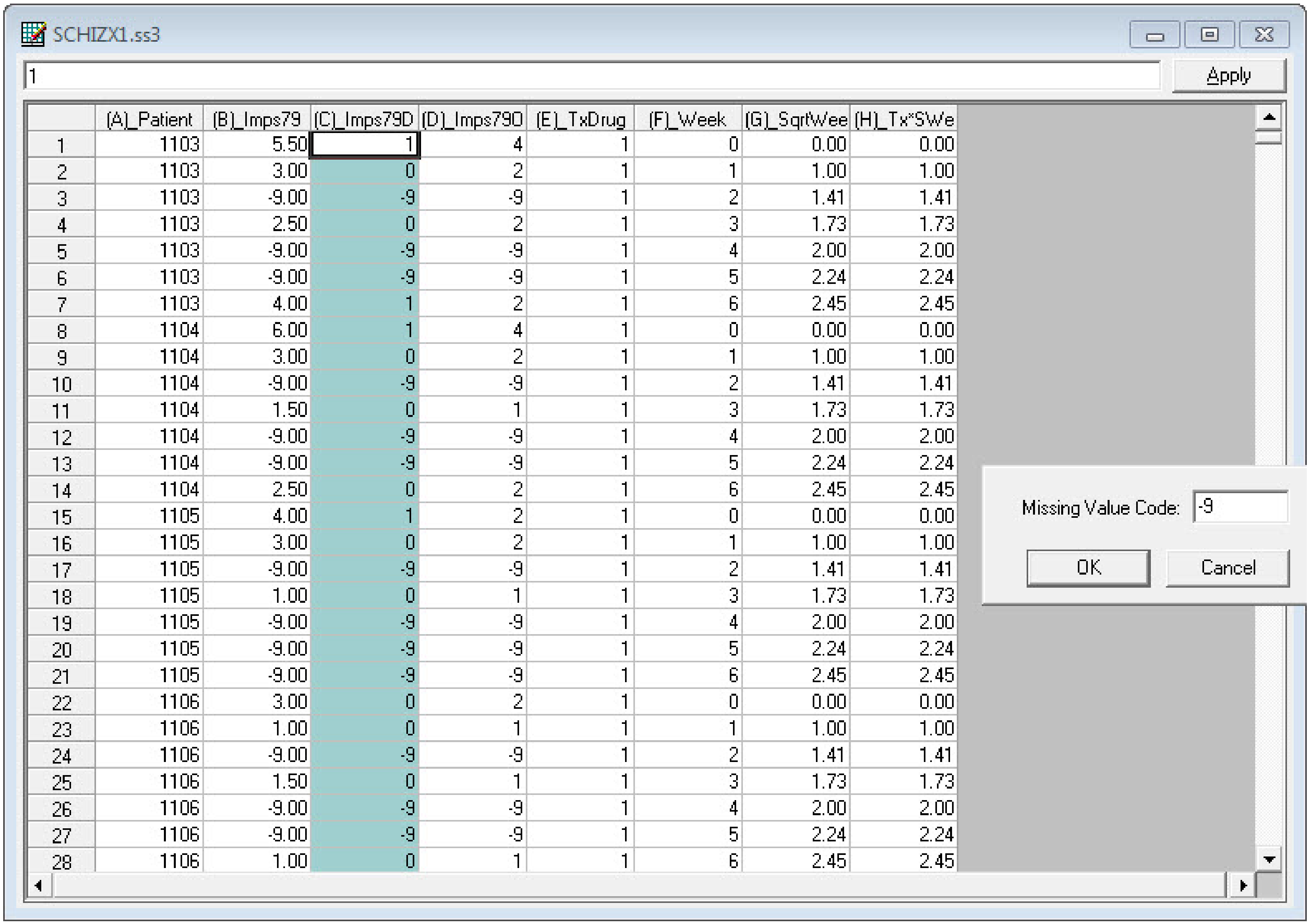
C:\SuperMixEn Examples\Workshop\Binary\SCHIZX1.ss3

SCHIZX1.ss3

1103 Apply

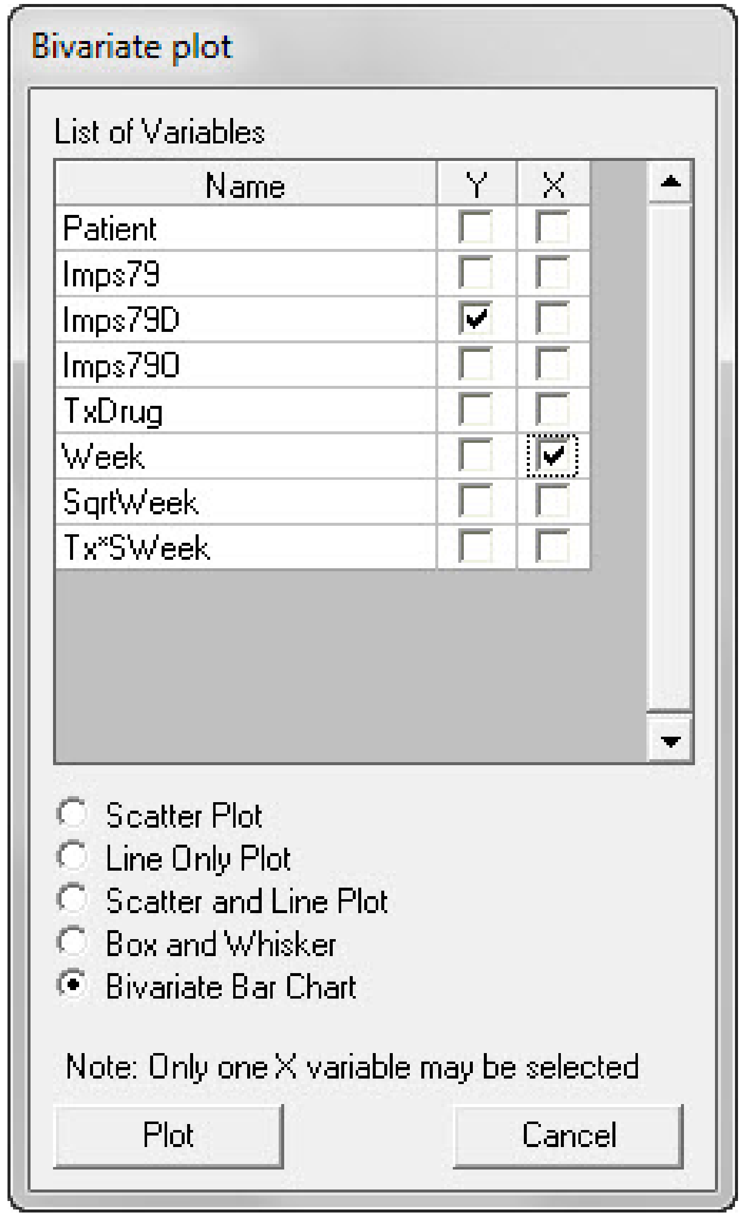
	(A)_Patient	(B)_Imps79	(C)_Imps79D	(D)_Imps790	(E)_TxDrug	(F)_Week	(G)_SqrtWee	(H)_Tx*SWe
1	1103	5.50	1	4	1	0	0.00	0.00
2	1103	3.00	0	2	1	1	1.00	1.00
3	1103	-9.00	-9	-9	1	2	1.41	1.41
4	1103	2.50	0	2	1	3	1.73	1.73
5	1103	-9.00	-9	-9	1	4	2.00	2.00
6	1103	-9.00	-9	-9	1	5	2.24	2.24
7	1103	4.00	1	2	1	6	2.45	2.45
8	1104	6.00	1	4	1	0	0.00	0.00
9	1104	3.00	0	2	1	1	1.00	1.00
10	1104	-9.00	-9	-9	1	2	1.41	1.41
11	1104	1.50	0	1	1	3	1.73	1.73
12	1104	-9.00	-9	-9	1	4	2.00	2.00
13	1104	-9.00	-9	-9	1	5	2.24	2.24
14	1104	2.50	0	2	1	6	2.45	2.45
15	1105	4.00	1	2	1	0	0.00	0.00
16	1105	3.00	0	2	1	1	1.00	1.00
17	1105	-9.00	-9	-9	1	2	1.41	1.41
18	1105	1.00	0	1	1	3	1.73	1.73
19	1105	-9.00	-9	-9	1	4	2.00	2.00
20	1105	-9.00	-9	-9	1	5	2.24	2.24
21	1105	-9.00	-9	-9	1	6	2.45	2.45
22	1106	3.00	0	2	1	0	0.00	0.00
23	1106	1.00	0	1	1	1	1.00	1.00
24	1106	-9.00	-9	-9	1	2	1.41	1.41
25	1106	1.50	0	1	1	3	1.73	1.73
26	1106	-9.00	-9	-9	1	4	2.00	2.00
27	1106	-9.00	-9	-9	1	5	2.24	2.24
28	1106	1.00	0	1	1	6	2.45	2.45

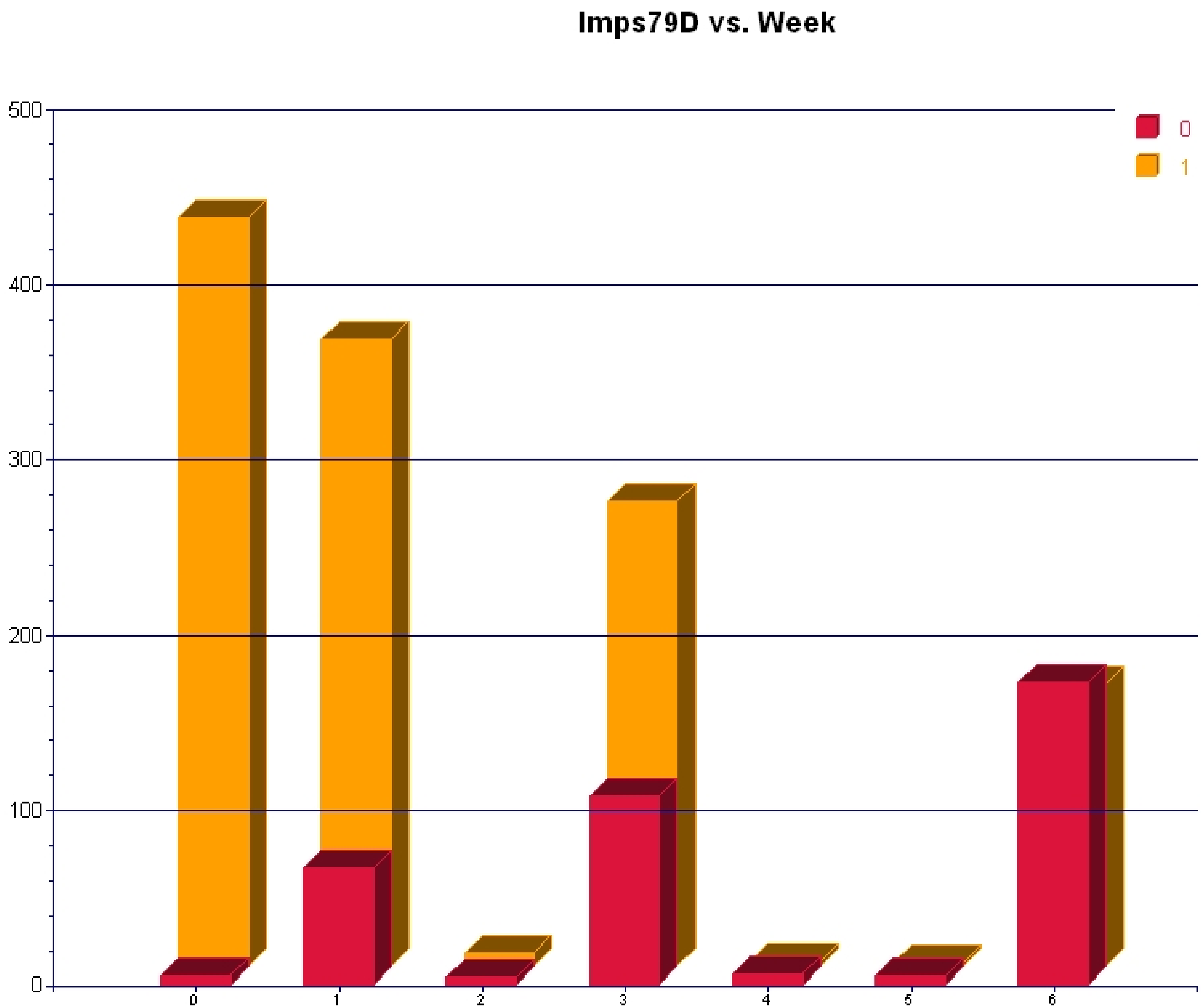
Select **`Imps79D`** column, then “Edit” > “Set Missing Value”



	(A)_Patient	(B)_Imps79	(C)_Imps79D	(D)_Imps79O	(E)_TxDrug	(F)_Week	(G)_SqrtWee	(H)_Tx*SWe
1	1103	5.50	1	4	1	0	0.00	0.00
2	1103	3.00	0	2	1	1	1.00	1.00
3	1103	-9.00	-9	-9	1	2	1.41	1.41
4	1103	2.50	0	2	1	3	1.73	1.73
5	1103	-9.00	-9	-9	1	4	2.00	2.00
6	1103	-9.00	-9	-9	1	5	2.24	2.24
7	1103	4.00	1	2	1	6	2.45	2.45
8	1104	6.00	1	4	1	0	0.00	0.00
9	1104	3.00	0	2	1	1	1.00	1.00
10	1104	-9.00	-9	-9	1	2	1.41	1.41
11	1104	1.50	0	1	1	3	1.73	1.73
12	1104	-9.00	-9	-9	1	4	2.00	2.00
13	1104	-9.00	-9	-9	1	5	2.24	2.24
14	1104	2.50	0	2	1	6	2.45	2.45
15	1105	4.00	1	2	1	0	0.00	0.00
16	1105	3.00	0	2	1	1	1.00	1.00
17	1105	-9.00	-9	-9	1	2	1.41	1.41
18	1105	1.00	0	1	1	3	1.73	1.73
19	1105	-9.00	-9	-9	1	4	2.00	2.00
20	1105	-9.00	-9	-9	1	5	2.24	2.24
21	1105	-9.00	-9	-9	1	6	2.45	2.45
22	1106	3.00	0	2	1	0	0.00	0.00
23	1106	1.00	0	1	1	1	1.00	1.00
24	1106	-9.00	-9	-9	1	2	1.41	1.41
25	1106	1.50	0	1	1	3	1.73	1.73
26	1106	-9.00	-9	-9	1	4	2.00	2.00
27	1106	-9.00	-9	-9	1	5	2.24	2.24
28	1106	1.00	0	1	1	6	2.45	2.45

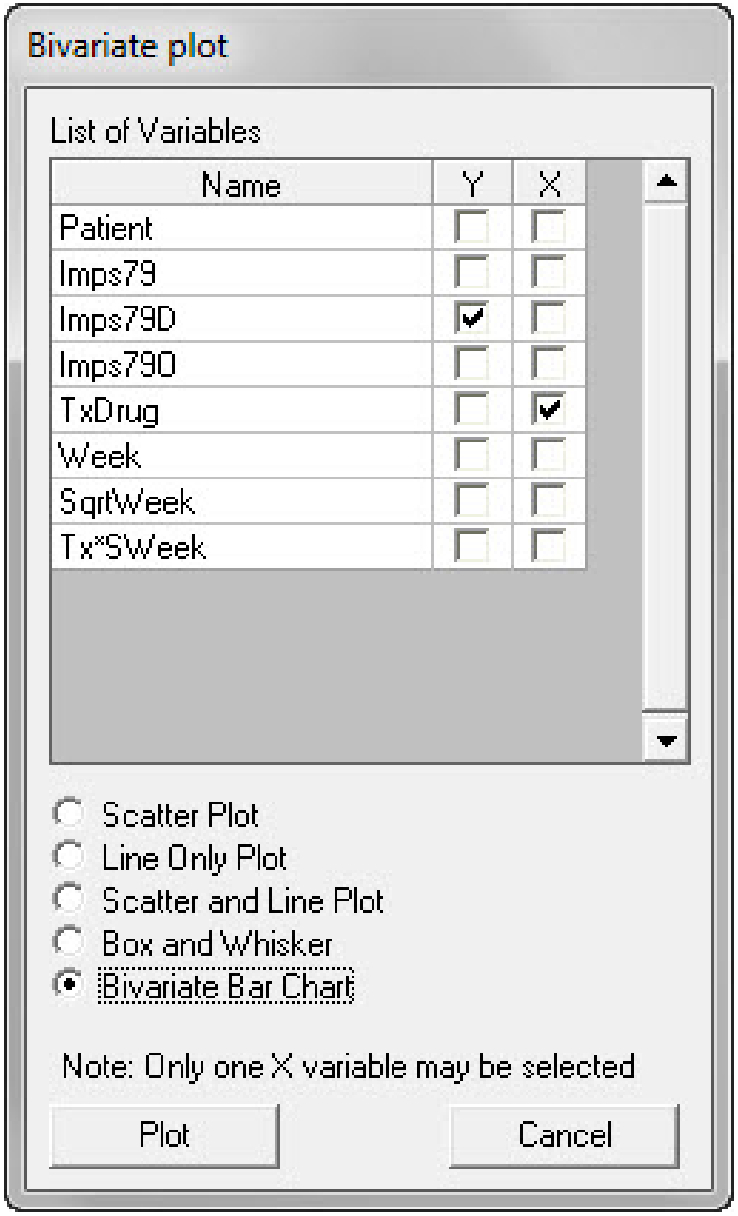
Select “File” > “Data-based Graphs” > “Bivariate”

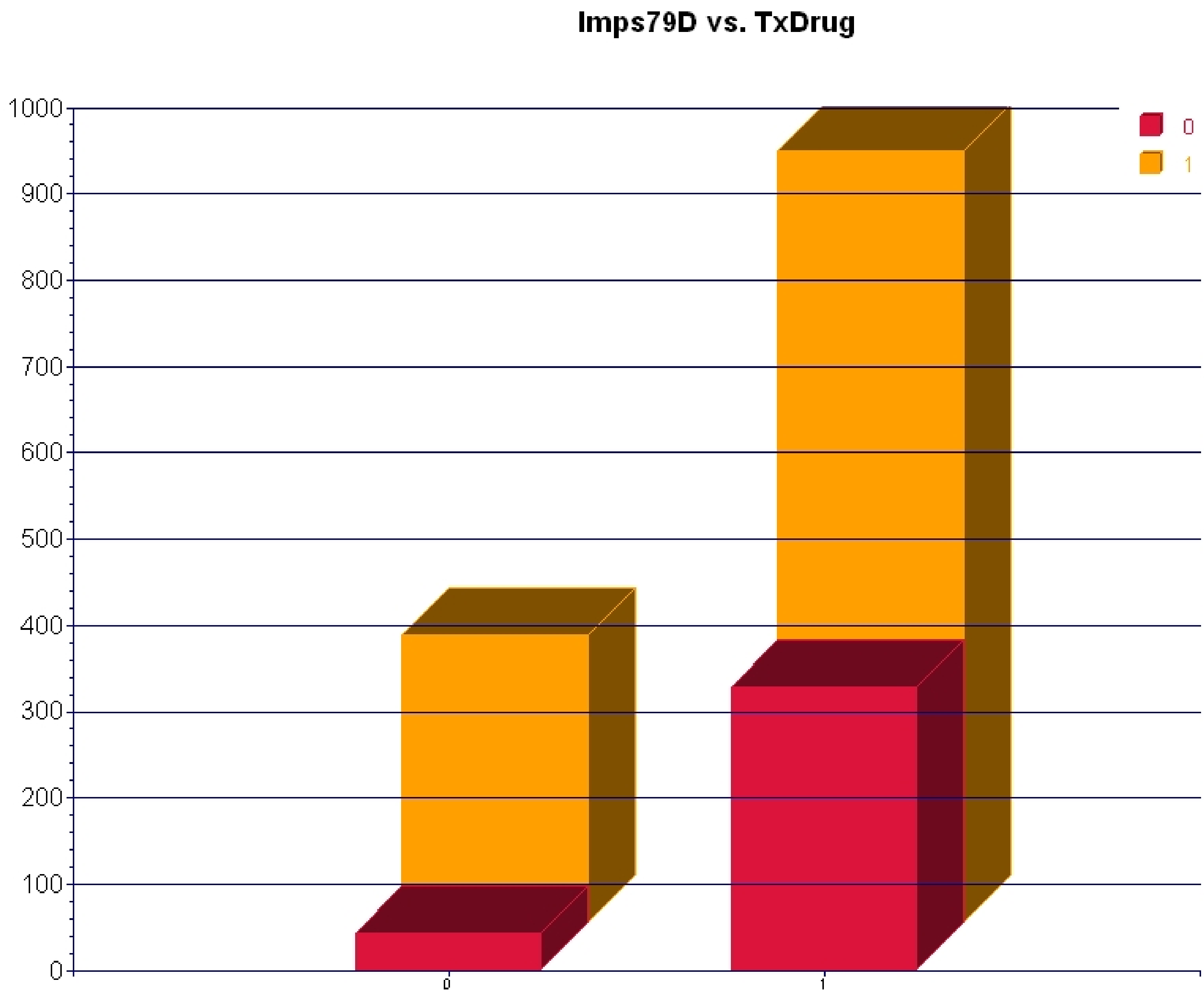




Imps79D vs. Week
500
400
300
200
100
0
0
1
2
3
4
5
6
0
1

Select “File” > “Data-based Graphs” > “Bivariate”





Imps79D vs. TxDrug
1000
900
800
700
600
500
400
300
200
100
0
0
1
0
1

Observed proportions $\geq$ "moderately ill"

	week 0	week 1	week 3	week 6
placebo	.98	.91	.89	.71
drug	.99	.82	.66	.42

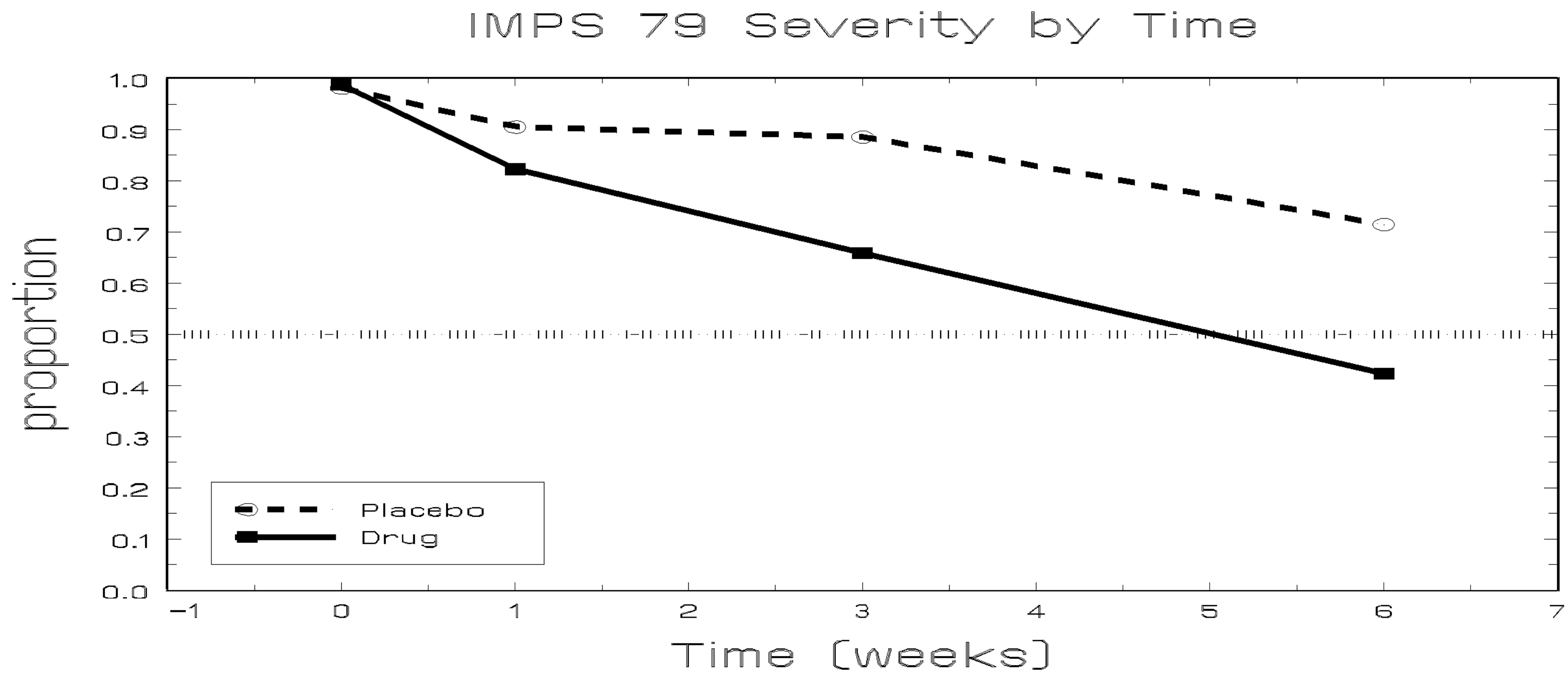
Observed odds $\geq$ "moderately ill"

	week 0	week 1	week 3	week 6
placebo	52.5	9.50	7.70	2.50
drug	80.8	4.63	1.93	.73
ratio	.65	2.05	3.99	3.42

Observed log odds $\geq$ "moderately ill"

	week 0	week 1	week 3	week 6
placebo	3.96	2.25	2.04	.92
drug	4.39	1.53	.66	-.31
difference	-.43	.72	1.38	1.23
exp (odds ratio)	.65	2.05	3.99	3.42

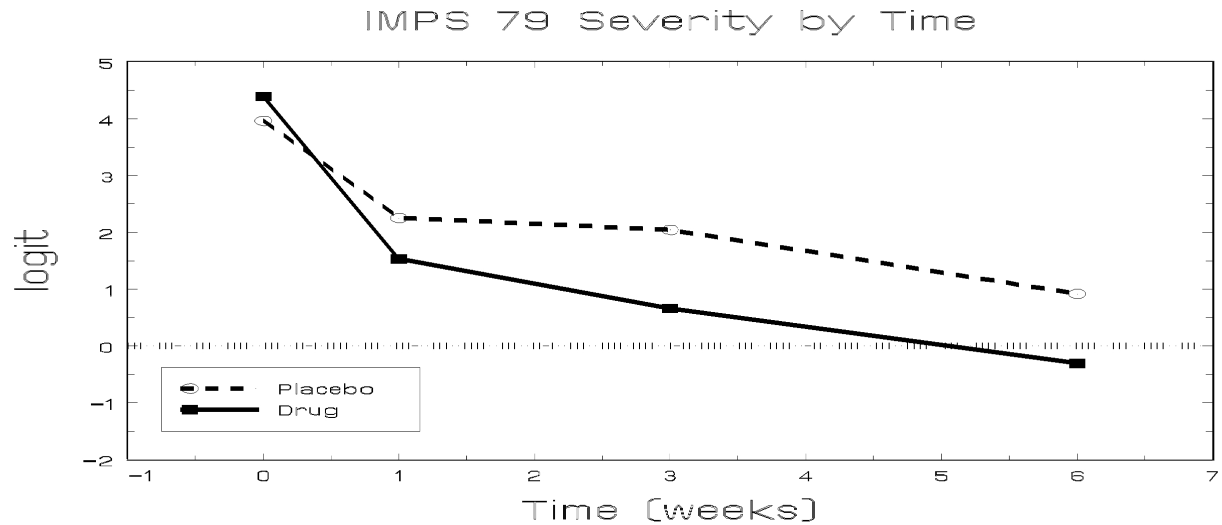
Observed Proportions across Time by Condition

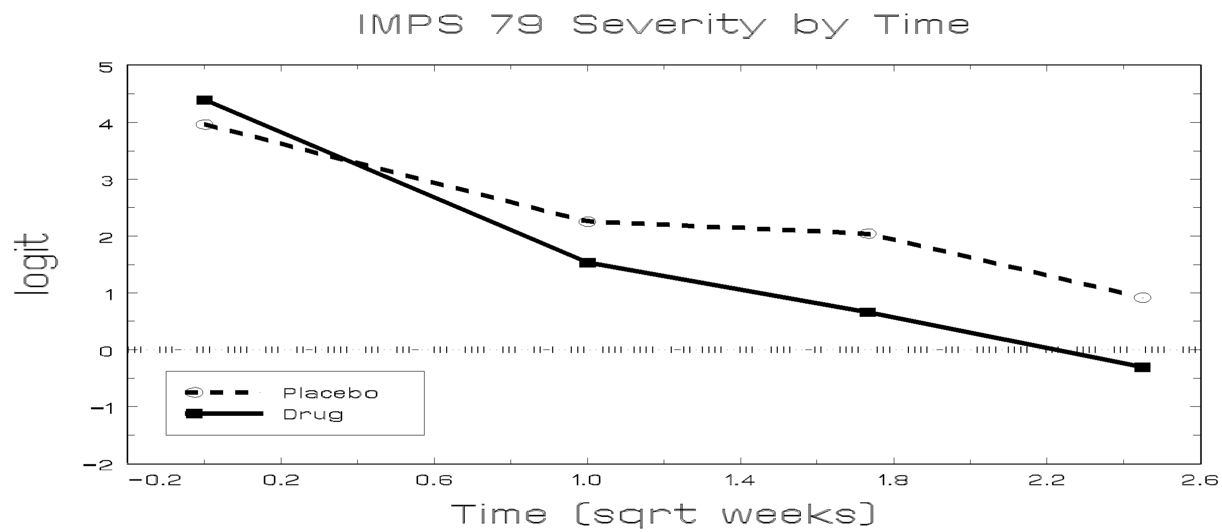


- model is not linear in terms of probabilities

$$P(Y_{ij} = 1 \mid v_{0i}) \; = \; \frac{1}{1 + \exp\left[-\left(\boldsymbol{x}'_{ij}\boldsymbol{\beta} + v_{0i}\right)\right]}$$

Observed Logits across Time by Condition





model is linear in terms of logits: $\log\left[\frac{P(Y_{ij}=1 \mid v_{0i})}{1-P(Y_{ij}=1 \mid v_{0i})}\right] = \boldsymbol{x}'_{ij}\boldsymbol{\beta} + v_{0i}$

Within-Subjects / Between-Subjects components

Within-subjects model - level 1 $(j = 1, \ldots, n_i \text{ obs})$

$$logit_{ij} = b_{0i} \; + \; b_{1i}\sqrt{Week}_j$$

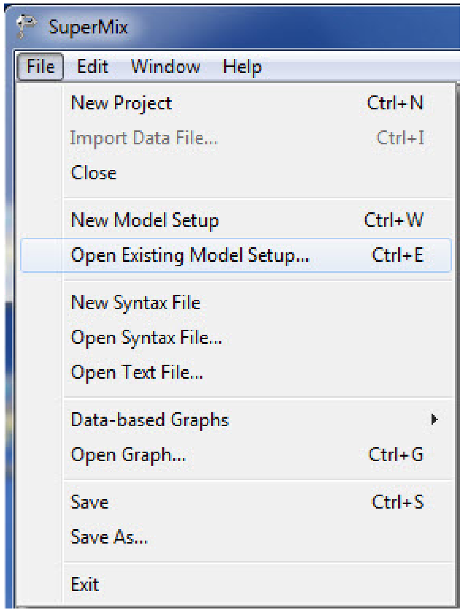
Between-subjects model - level 2 $(i = 1, \ldots, N \text{ subjects})$

$$b_{0i} \; = \; \beta_0 \; + \; \beta_2 Grp_i \; + \; \upsilon_{0i}$$

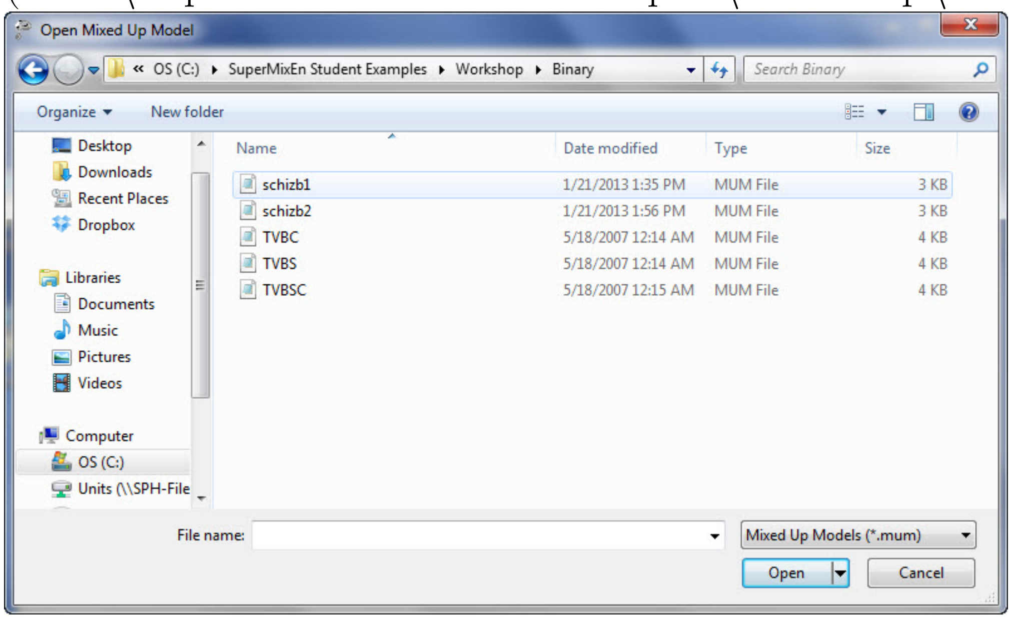
$$b_{1i} \; = \; \beta_1 \; + \; \beta_3 Grp_i$$

$$\upsilon_{0i} \sim \mathcal{NID}(0, \sigma_\upsilon^2)$$

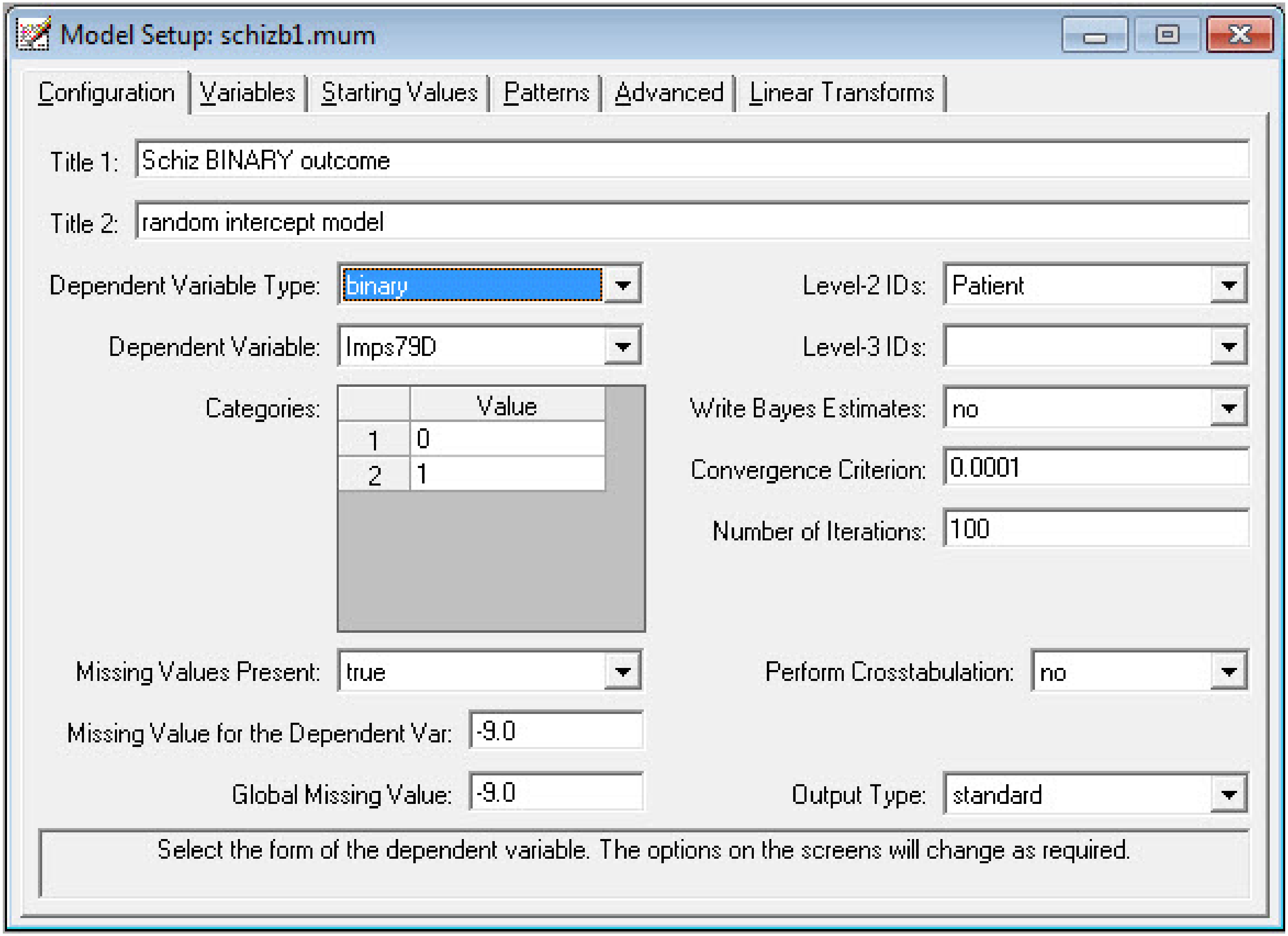
Under "File" click on "Open Existing Model Setup"

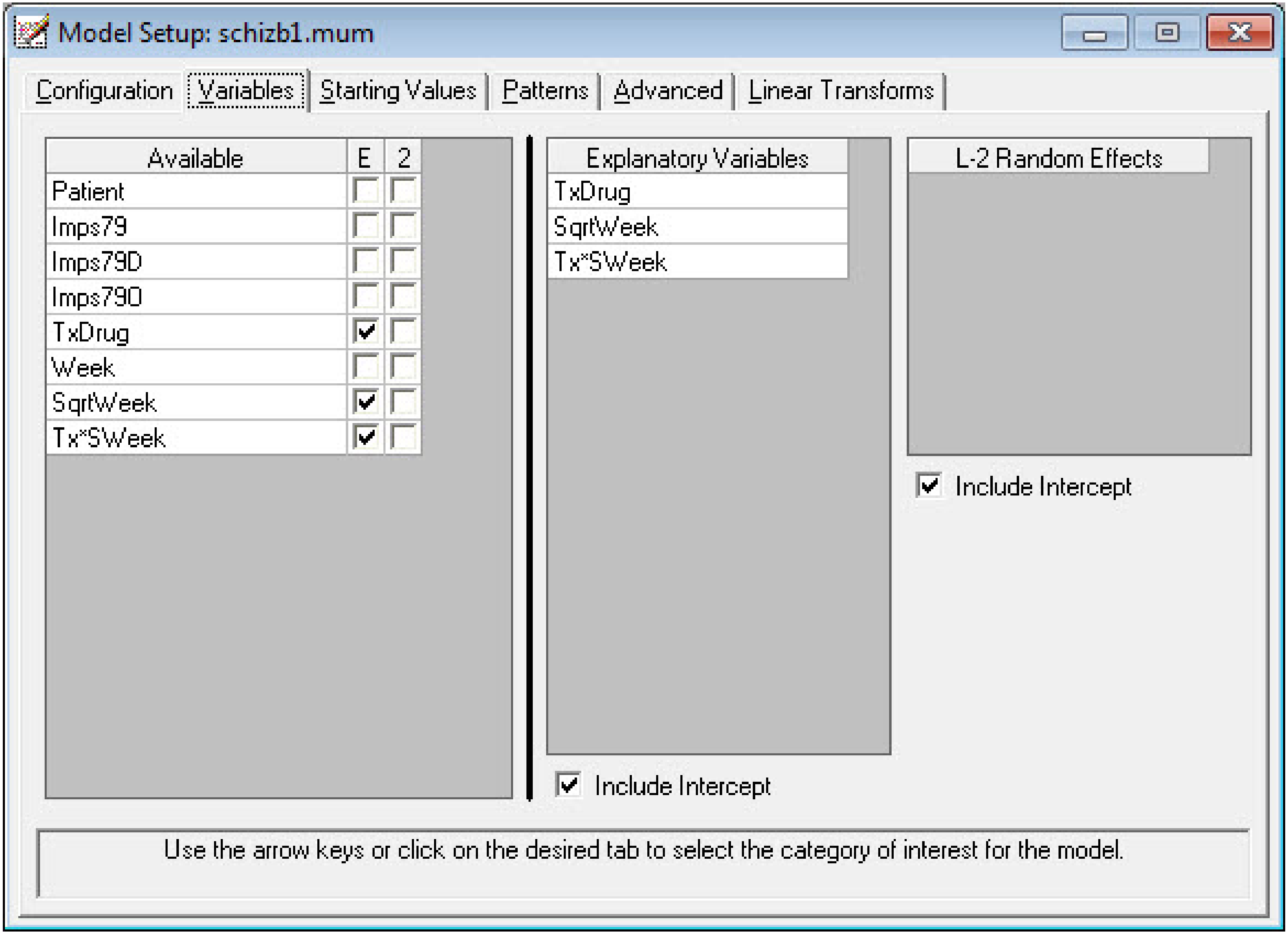


Open C:\SuperMixEn Examples\Workshop\Binary\schizb1.mum
(or C:\SuperMixEn Student Examples\Workshop\Binary\schizb1.mum)



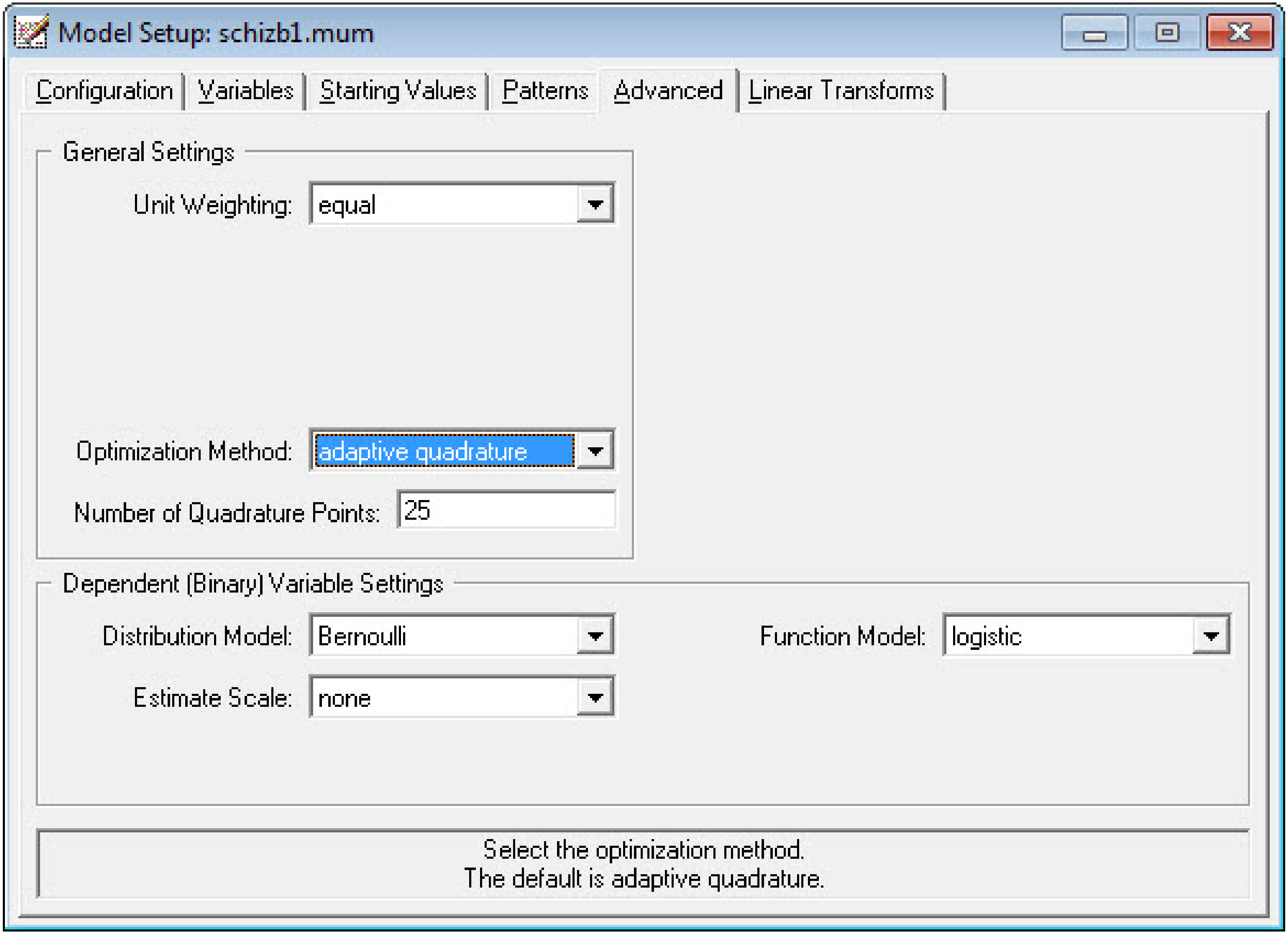
Note “Dependent Variable Type” should be “binary”





Model Setup: schizb1.mum
Configuration
Variables
Starting Values
Patterns
Advanced
Linear Transforms
Available
E
2
Patient
Imps79
Imps79D
Imps79O
TxDrug
Week
SqrtWeek
Tx*SWeek
Explanatory Variables
TxDrug
SqrtWeek
Tx*SWeek
L-2 Random Effects
Include Intercept
Include Intercept
Use the arrow keys or click on the desired tab to select the category of interest for the model.

Note "Optimization Method" should be "adaptive quadrature"



schizb1.out

```
| Schiz BINARY outcome    |
| random intercept model |
o========================o



           Model and Data Descriptions

   Sampling Distribution                     = Bernoulli
   Link Function                             = Logistic
   PROB(Success)= 1.0/[1.0+EXP(-ETA)]

   Number of Level-2 Units                     437
   Number of Level-1 Units                     1603
   Number of Level-1 Units per Level-2 Unit =
     4     4     3     4     4     4     4     4     4     3     4     4
     4     2     3     4     3     4     3     4     4     4     3     3
     2     4     4     4     4     4     3     4     4     4     4     4
     4     4     4     4     2     3     4     3     4     4     4     3
     4     4     2     2     4     5     4     2     4     4     3     4
     4     3     2     3     4     4     4     4     4     4     2     4
     4     4     5     4     4     2     2     4     2     4     4     3
     3     4     4     4     4     4     4     4     4     3     3     4
     2     3     4     4     4     2     5     3     4     4     2     4
     4     4     2     4     4     4     4     4     4     4     4     4
     5     2     4     3     4     4     2     2     4     4     4     4
     4     2     4     4     4     4     4     4     4     4     4     4
     4     4     4     2     4     4     2     4     4     4     3     4
     2     4     4     3     2     3     4     4     3     3     4     3
     4     4     4     4     4     4     4     4     4     4     4     4
     4     4     2     3     3     5     4     3     4     4     3     2
     4     4     4     4     4     3     3     4     4     4     4     4
     4     4     4     4     4     4     4     4     4     4     3     4
     4     4     4     4     4     2     3     4     4     4     2     4
     4     4     4     3     4     4     4     4     4     4     4     4
     3     4     4     3     4     4     2     4     4     4     4     2
     4     4     4     2     4     4     4     3     3     4     3     4
     2     4     4     4     3     3     4     4     4     4     3     3
     4     3     4     4     4     4     4     3     4     4     4     4
     4     3     3     4     2     4     4     4     4     4     4     4
     4     3     4     4     3     3     4     2     4     3     3     3
     4     4     4     4     4     4     4     3     2     3     4     4
```

Save As... Close

schizb1.out

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

Number of quadrature points =	25
Number of free parameters =	5
Number of iterations used =	6
-2lnL (deviance statistic) =	1249.73465
Akaike Information Criterion	1259.73465
Schwarz Criterion	1286.63281

Estimated regression weights

Parameter	Estimate	Standard Error	z Value	P Value
intercept	5.3851	0.6303	8.5432	0.0000
TxDrug	-0.0247	0.6533	-0.0378	0.9698
SqrtWeek	-1.4996	0.2906	-5.1606	0.0000
Tx*SWeek	-1.0143	0.3338	-3.0385	0.0024

Odds Ratio and 95% Odds Ratio Confidence Intervals

Parameter	Estimate	Odds Ratio	Bounds Lower	Bounds Upper
intercept	5.3851	218.1386	63.4125	750.3956
TxDrug	-0.0247	0.9756	0.2711	3.5106
SqrtWeek	-1.4996	0.2232	0.1263	0.3945
Tx*SWeek	-1.0143	0.3627	0.1885	0.6977

Estimated level 2 variances and covariances

Parameter	Estimate	Standard Error	z Value	P Value
intercept/intercept	4.4781	0.9458	4.7345	0.0000

schizb1.out

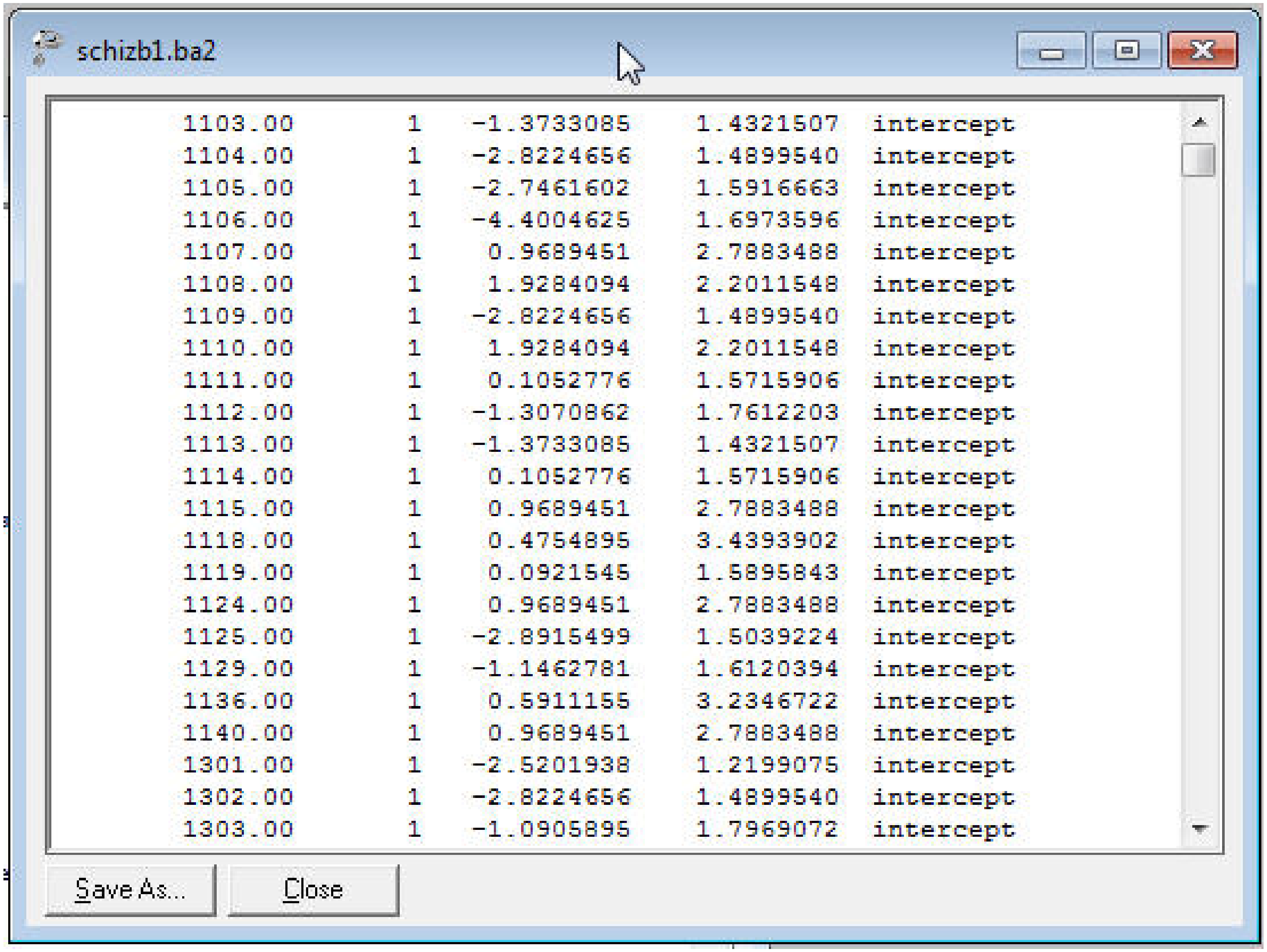
```
Calculation of the intracluster correlation
-------------------------------------------
residual variance = pi*pi / 3 (assumed)
cluster  variance =     4.4781

intracluster correlation =     4.4781 / (     4.4781 + (pi*pi/3)) = 0.576


                        Population Average Estimates

                                                  Standard
   Parameter                Estimate              Error        z Value      P Value
   ---------                --------              --------     -------      -------
   intercept                  3.5427                0.4628      7.6549       0.0000
   TxDrug                    -0.0546                0.5162     -0.1058       0.9157
   SqrtWeek                  -1.0503                0.2238     -4.6936       0.0000
   Tx*SWeek                  -0.5964                0.2502     -2.3838       0.0171


       Odds Ratio and 95% Odds Ratio Confidence Intervals

                                                                     Bounds
   Parameter                Estimate            Odds Ratio      Lower        Upper
   ---------                --------            ----------      -----        -----
   intercept                  3.5427               34.5605    13.9519      85.6102
   TxDrug                    -0.0546                0.9468     0.3443       2.6040
   SqrtWeek                  -1.0503                0.3498     0.2256       0.5424
   Tx*SWeek                  -0.5964                0.5508     0.3373       0.8994


    o=================================o
    | SuperMix used 0.31 seconds CPU |
    o=================================o
```

Save As... Close

SuperMix is FAST for full-likelihood estimation of non-normal models, and up to three level models

Empirical Bayes Estimates of Random Effects

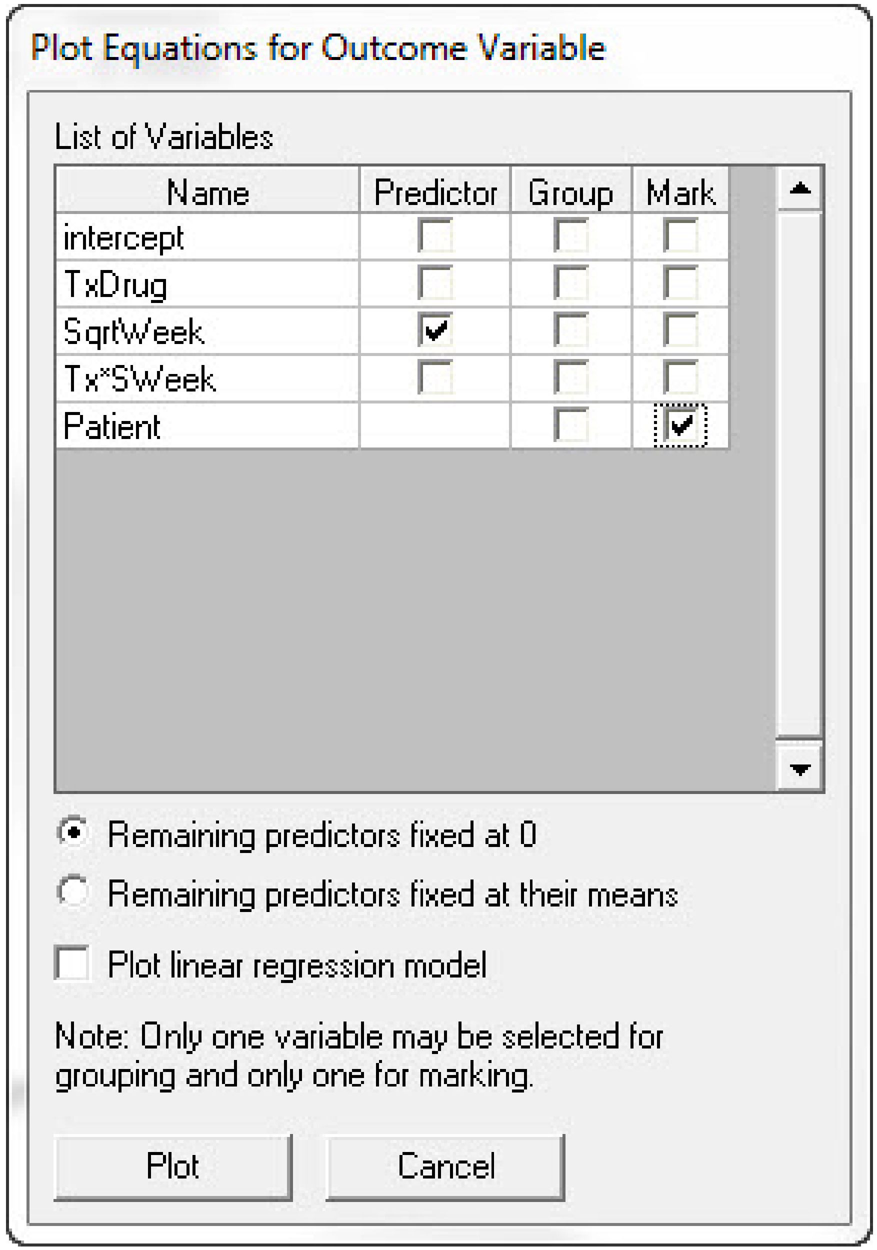
Select “Analysis” > “View Level-2 Bayes Results”

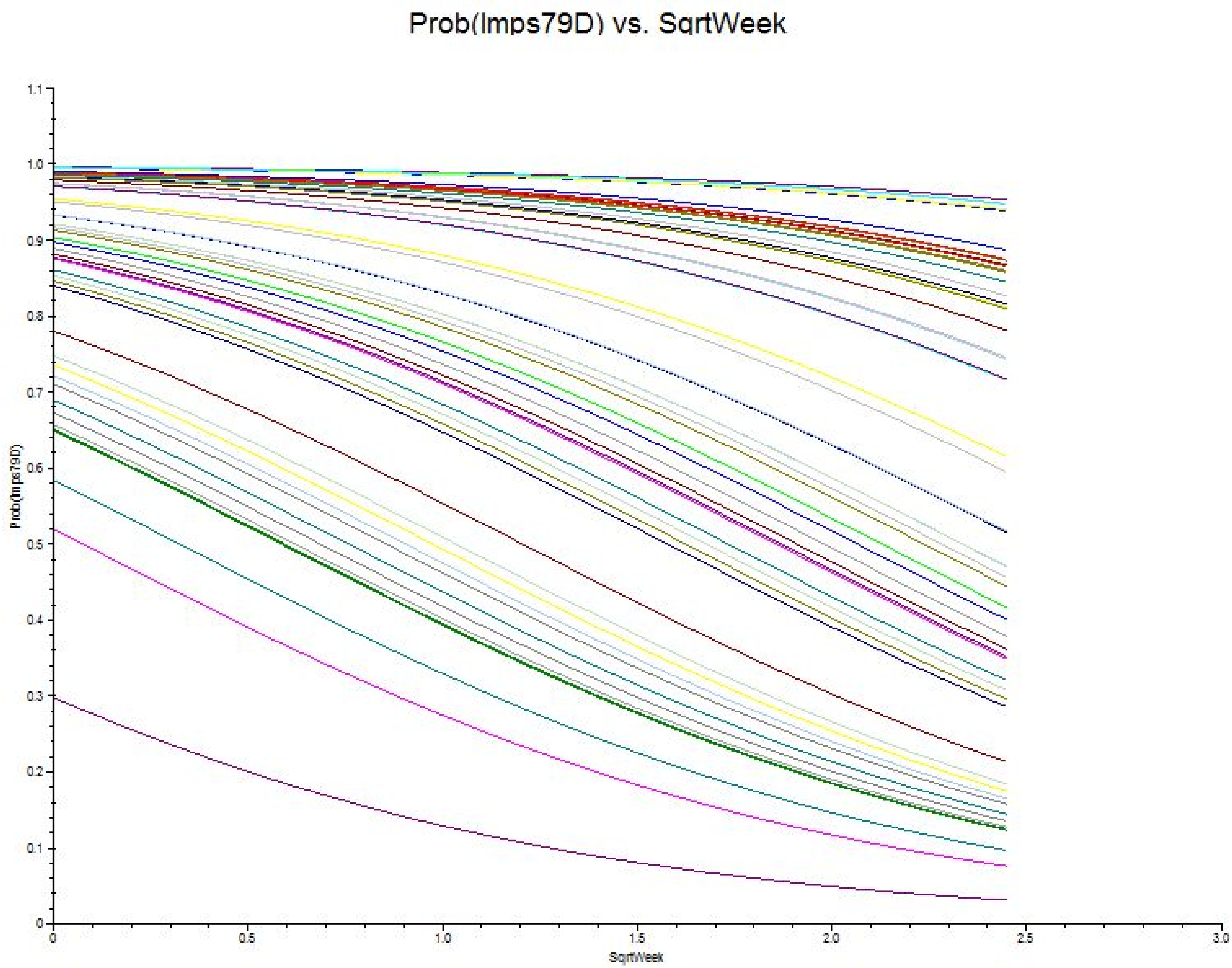


1103.00	1	-1.3733085	1.4321507	intercept
1104.00	1	-2.8224656	1.4899540	intercept
1105.00	1	-2.7461602	1.5916663	intercept
1106.00	1	-4.4004625	1.6973596	intercept
1107.00	1	0.9689451	2.7883488	intercept
1108.00	1	1.9284094	2.2011548	intercept
1109.00	1	-2.8224656	1.4899540	intercept
1110.00	1	1.9284094	2.2011548	intercept
1111.00	1	0.1052776	1.5715906	intercept
1112.00	1	-1.3070862	1.7612203	intercept
1113.00	1	-1.3733085	1.4321507	intercept
1114.00	1	0.1052776	1.5715906	intercept
1115.00	1	0.9689451	2.7883488	intercept
1118.00	1	0.4754895	3.4393902	intercept
1119.00	1	0.0921545	1.5895843	intercept
1124.00	1	0.9689451	2.7883488	intercept
1125.00	1	-2.8915499	1.5039224	intercept
1129.00	1	-1.1462781	1.6120394	intercept
1136.00	1	0.5911155	3.2346722	intercept
1140.00	1	0.9689451	2.7883488	intercept
1301.00	1	-2.5201938	1.2199075	intercept
1302.00	1	-2.8224656	1.4899540	intercept
1303.00	1	-1.0905895	1.7969072	intercept

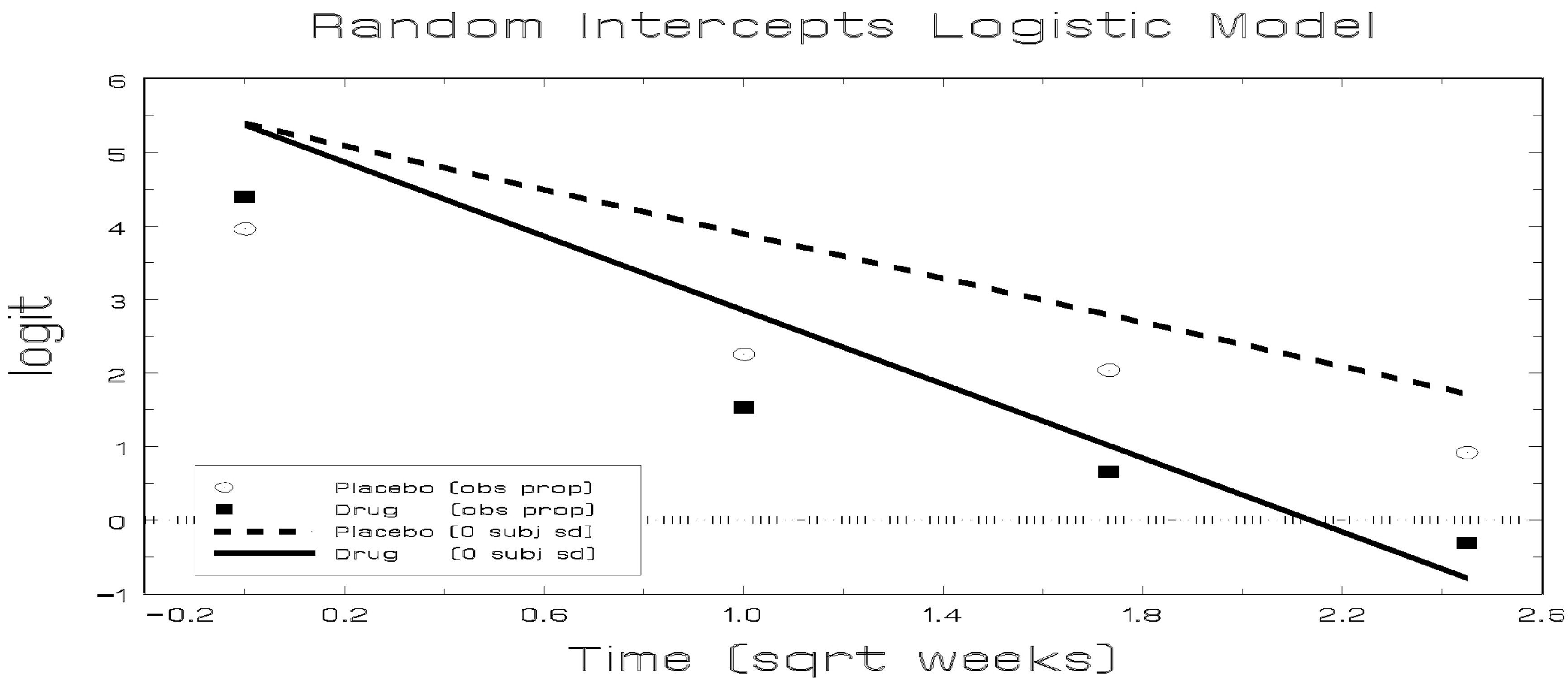
ID, random effect number, estimate, variance, name

Close output, select “File” > “Model-based Graphs” > “Equations”




Prob(Imps79D) vs. SqrtWeek
Prob(Imps79D)
SqrtWeek
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0.5
1.0
1.5
2.0
2.5
3.0

Estimated (subject-specific) Logits across Time by Condition: *random-intercepts model*



$$\log\left[\frac{P(Y_{ij}=1 \mid \upsilon_{0i})}{1-P(Y_{ij}=1 \mid \upsilon_{0i})}\right] = 5.39 - .025\,D_i - 1.50\,T_j - 1.01\,(D_i \times T_j) + \upsilon_{0i}$$

$$\upsilon_{0i} \sim \mathcal{NID}(0, \hat{\sigma}_\upsilon^2 = 4.48)$$

$\hat{\boldsymbol{\beta}}$ change in (conditional) logit due to $\boldsymbol{x}$ for subjects with the same value of υ_{0i} (the above plot is for $\upsilon_{0i} = 0$)

Random-intercepts Logistic Regression

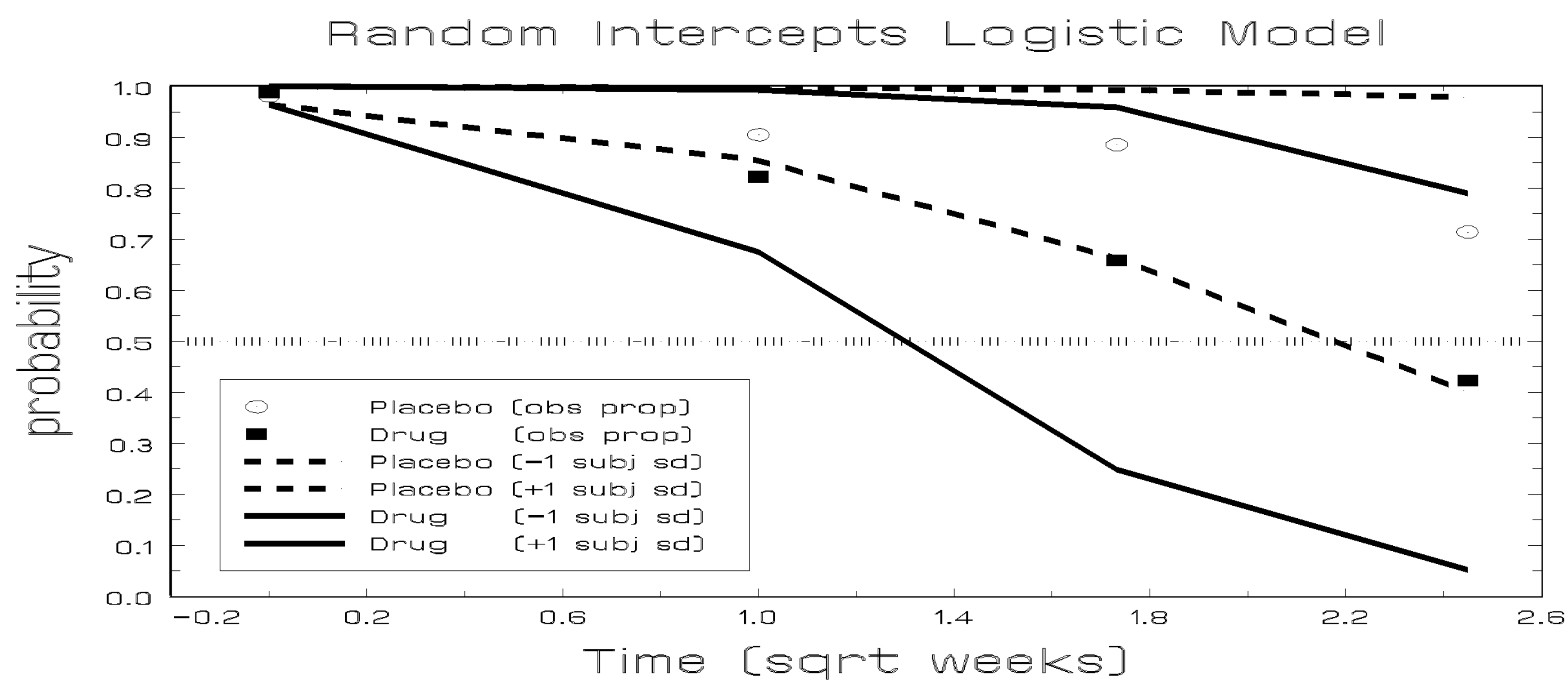
$$logit_{ij} = \boldsymbol{x}'_{ij}\boldsymbol{\beta} + v_{0i}$$

- every subject has their own propensity for response (v_{0i})
- the influence of covariates $\boldsymbol{x}$ is determined controlling (or adjusting) for the subject effect
- the covariance structure, or dependency, of the repeated observations is explicitly modeled

$$\begin{aligned}\beta_0 &= \text{log odds of response for a typical subject with } \boldsymbol{x} = 0 \text{ and } \\ &\quad\; \upsilon_{0i} = 0 \\ \boldsymbol{\beta} &= \text{log odds ratio for response associated with unit changes in} \\ &\quad\; \boldsymbol{x} \text{ for the same subject value } \upsilon_{0i} \\ &\quad\; * \text{ referred to as ``subject-specific''} \\ &\quad\; * \text{ how a } \textit{subject's} \text{ response probability depends on } \boldsymbol{x} \\ \sigma_\upsilon^2 &= \text{degree of heterogeneity across subjects in the probability} \\ &\quad\; \text{of response not attributable to } \boldsymbol{x}\end{aligned}$$

- most useful when the objective is to make inference about *subjects* rather than the population average
- interest is in the heterogeneity of subjects

Estimated Subject-Specific Probabilites



$$P(Y_{ij} = 1 \mid v_{0i}) = \frac{1}{1 + \exp\left[-\left(5.39 - .03\,D_i - 1.50\,T_j - 1.01\,D_i T_j + v_{0i}\right)\right]}$$

$$\text{where } v_{0i} = \begin{cases} -1\sigma_v \\ \;\;1\sigma_v \end{cases} \text{ and } \hat{\sigma}_v = 2.12$$

Instead of the mixed model, consider the following marginal model

$$\log\left[\frac{P(Y_{ij}=1)}{1-P(Y_{ij}=1)}\right] = \boldsymbol{x}'_{ij}\boldsymbol{\beta}^{pa}$$

- $\boldsymbol{\beta}^{pa}$ have marginal or "population-average" interpretation
- Not conditional on subject random effects
- Estimates from a GEE model are of this type
- $\boldsymbol{\beta}^{ss} \neq \boldsymbol{\beta}^{pa}$ unless random effect variance(s) equal 0 (or $\beta = 0$)

$\Rightarrow$ Can one obtain $\boldsymbol{\beta}^{pa}$ from $\boldsymbol{\beta}^{ss}$?

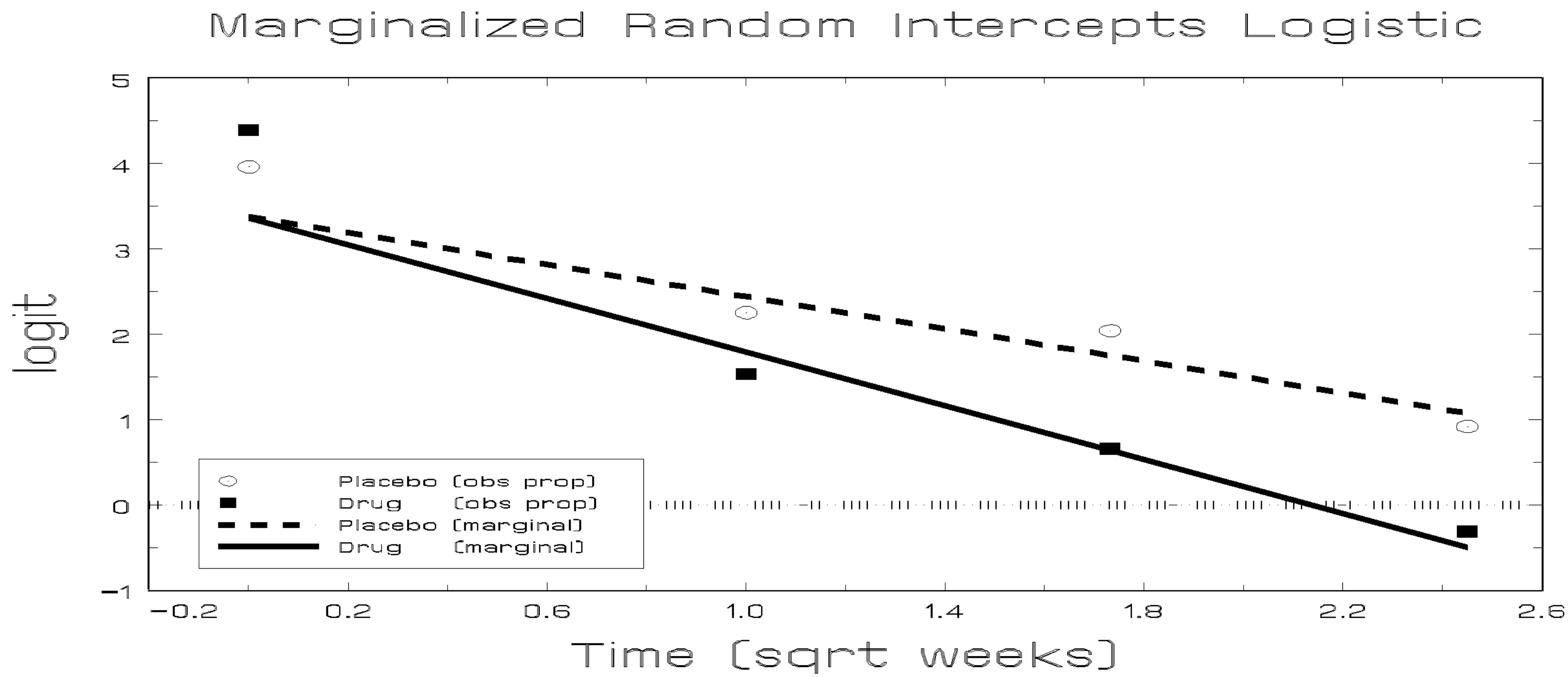
For a random-intercept model with estimates $\hat{\boldsymbol{\beta}}^{ss}$ and $\hat{\sigma}_v^2$

$$\hat{\boldsymbol{\beta}}^{pa} \approx \hat{\boldsymbol{\beta}}^{ss} \Big/ \sqrt{\frac{\hat{\sigma}_v^2 + \pi^2/3}{\pi^2/3}}$$

- $\pi^2/3$ is the variance of the standard logistic distribution
- square-root term on the right-hand side can be viewed as the "marginalization" factor; transforms subject-specific parameters into their population-averaged counterparts
- In a random-intercepts model, the variance is equal across time; marginalization factor is equal across time and is a scalar
- For models with multiple random effects, this is not the case and so there is no simple relationship

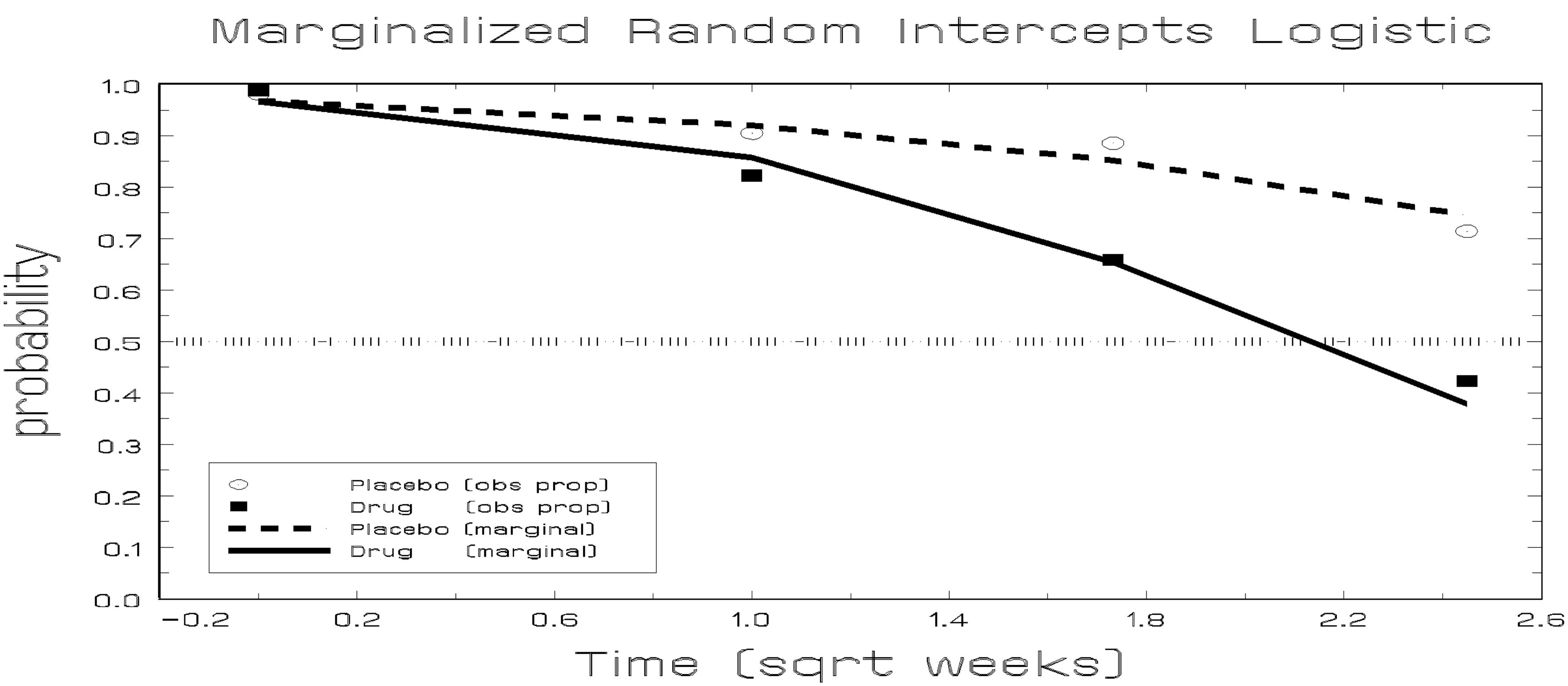
- Hedeker, du Toit, Demirtas, Gibbons (2014) describe a general marginalization approach that has been implemented in the update of Supermix to yield Population Average Estimates

```
schizb1.out

Calculation of the intracluster correlation
-------------------------------------------
residual variance = pi*pi / 3 (assumed)
cluster  variance =     4.4781

intracluster correlation =     4.4781 / (    4.4781 + (pi*pi/3)) = 0.576


                      Population Average Estimates

                                          Standard
   Parameter              Estimate         Error      z Value     P Value
   ---------              --------        --------    -------     -------
   intercept                3.5427          0.4628     7.6549      0.0000
   TxDrug                  -0.0546          0.5162    -0.1058      0.9157
   SqrtWeek                -1.0503          0.2238    -4.6936      0.0000
   Tx*SWeek                -0.5964          0.2502    -2.3838      0.0171


       Odds Ratio and 95% Odds Ratio Confidence Intervals

                                                            Bounds
   Parameter              Estimate       Odds Ratio     Lower        Upper
   ---------              --------       ----------     -----        -----
   intercept                3.5427          34.5605    13.9519      85.6102
   TxDrug                  -0.0546           0.9468     0.3443       2.6040
   SqrtWeek                -1.0503           0.3498     0.2256       0.5424
   Tx*SWeek                -0.5964           0.5508     0.3373       0.8994



    o=================================o
    | SuperMix used 0.31 seconds CPU  |
    o=================================o

Save As...    Close
```



$$\log\left[\frac{P(Y_{ij}=1)}{1-P(Y_{ij}=1)}\right] = 3.54 - .055\,D_i - 1.05\,T_j - .60\,(D_i \times T_j)$$

$\Rightarrow$ these are the Population Average Estimates from Supermix



$$P(Y_{ij} = 1) = \frac{1}{1 + \exp\left[-\left(3.54 - .055\, D_i - 1.05\, T_j - .60\, D_i T_j\right)\right]}$$

$\Rightarrow$ these are the Population Average Estimates from Supermix

Within-Subjects / Between-Subjects components

Within-subjects model - *level 1* $\quad (j = 1, \ldots, n_i \text{ obs})$

$$logit_{ij} = b_{0i} \; + \; b_{1i}\sqrt{Week}_j$$

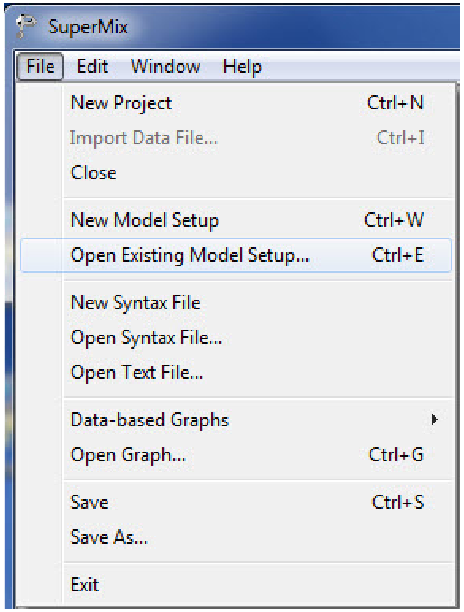
Between-subjects model - *level 2* $\quad (i = 1, \ldots, N \text{ subjects})$

$$b_{0i} \; = \; \beta_0 \; + \; \beta_2 Grp_i \; + \; \upsilon_{0i}$$

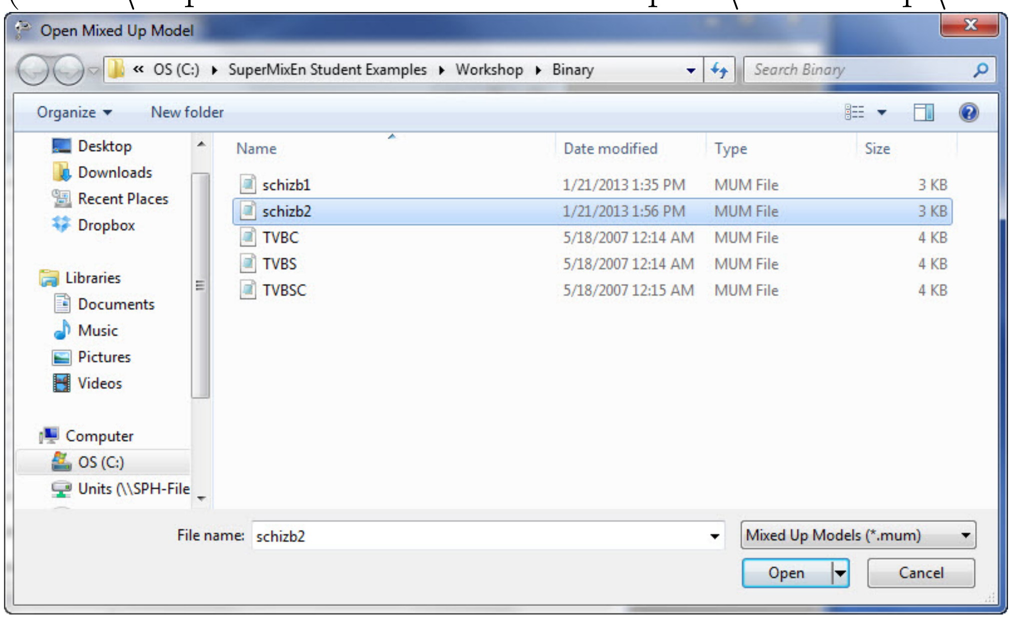
$$b_{1i} \; = \; \beta_1 \; + \; \beta_3 Grp_i \; + \; \upsilon_{1i}$$

$$\boldsymbol{\upsilon}_i \sim \mathcal{NID}(\mathbf{0}, \mathbf{\Sigma}_\upsilon)$$

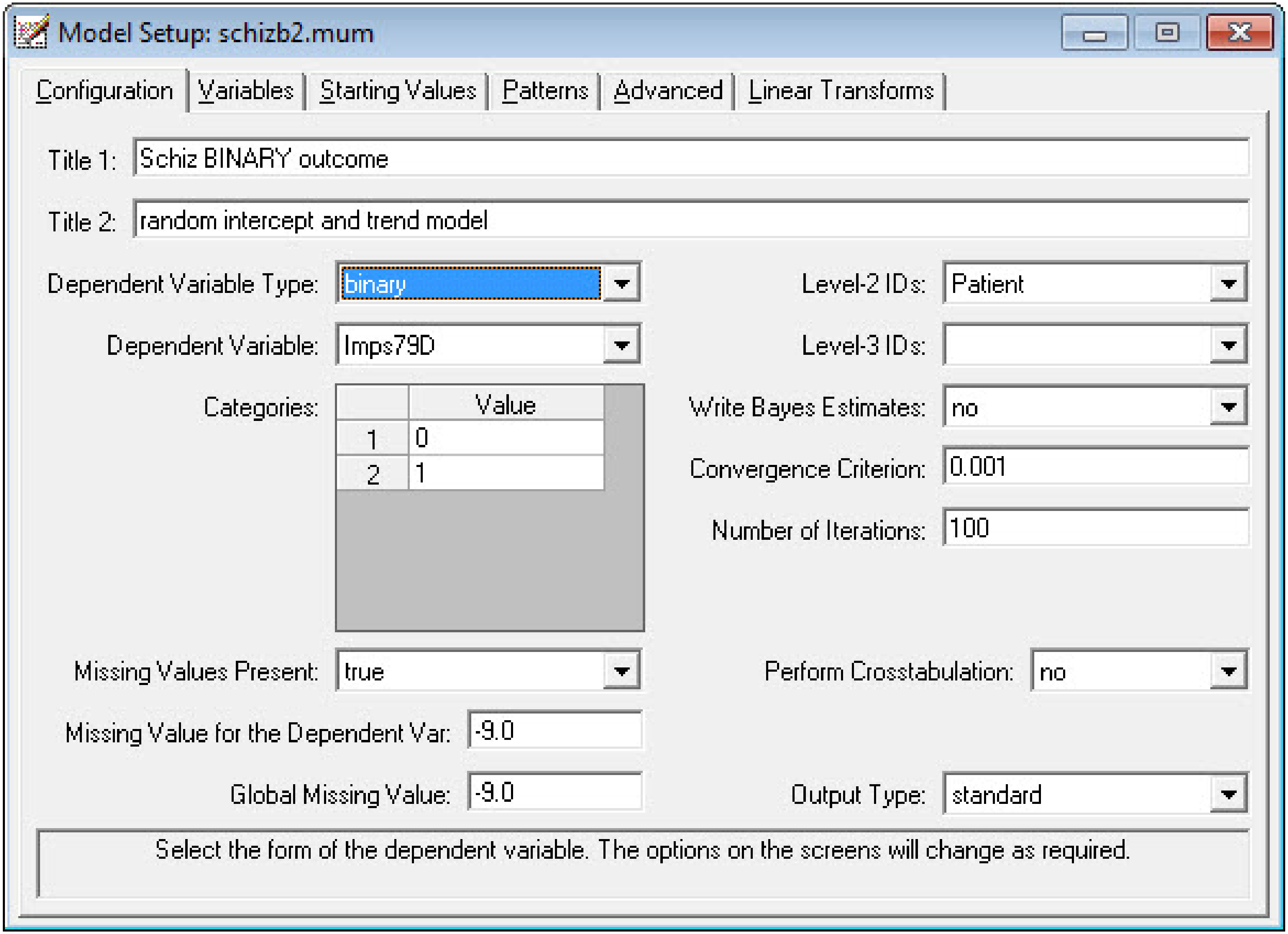
Under "File" click on "Open Existing Model Setup"



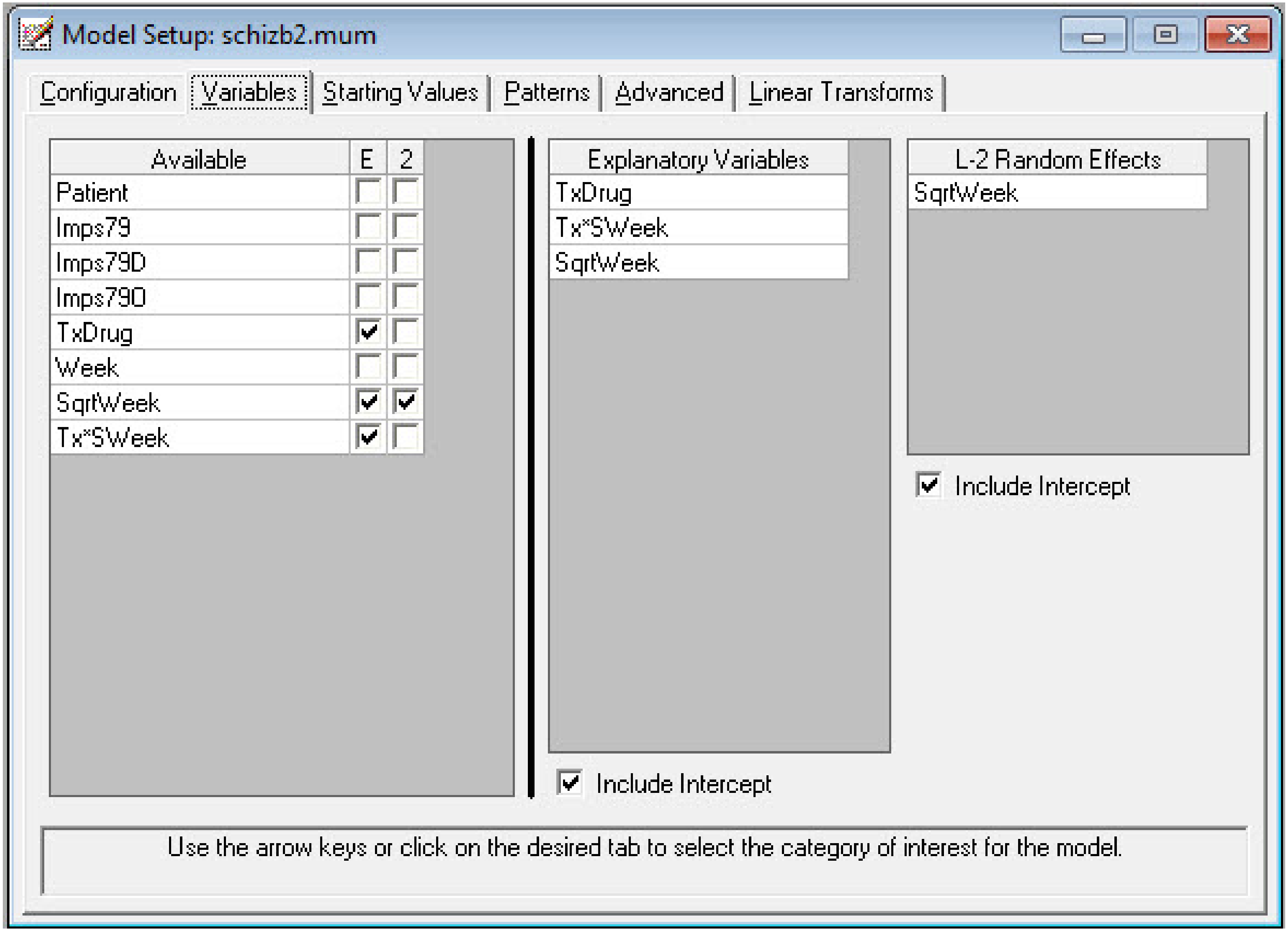
Open C:\SuperMixEn Examples\Workshop\Binary\schizb2.mum
(or C:\SuperMixEn Student Examples\Workshop\Binary\schizb2.mum)



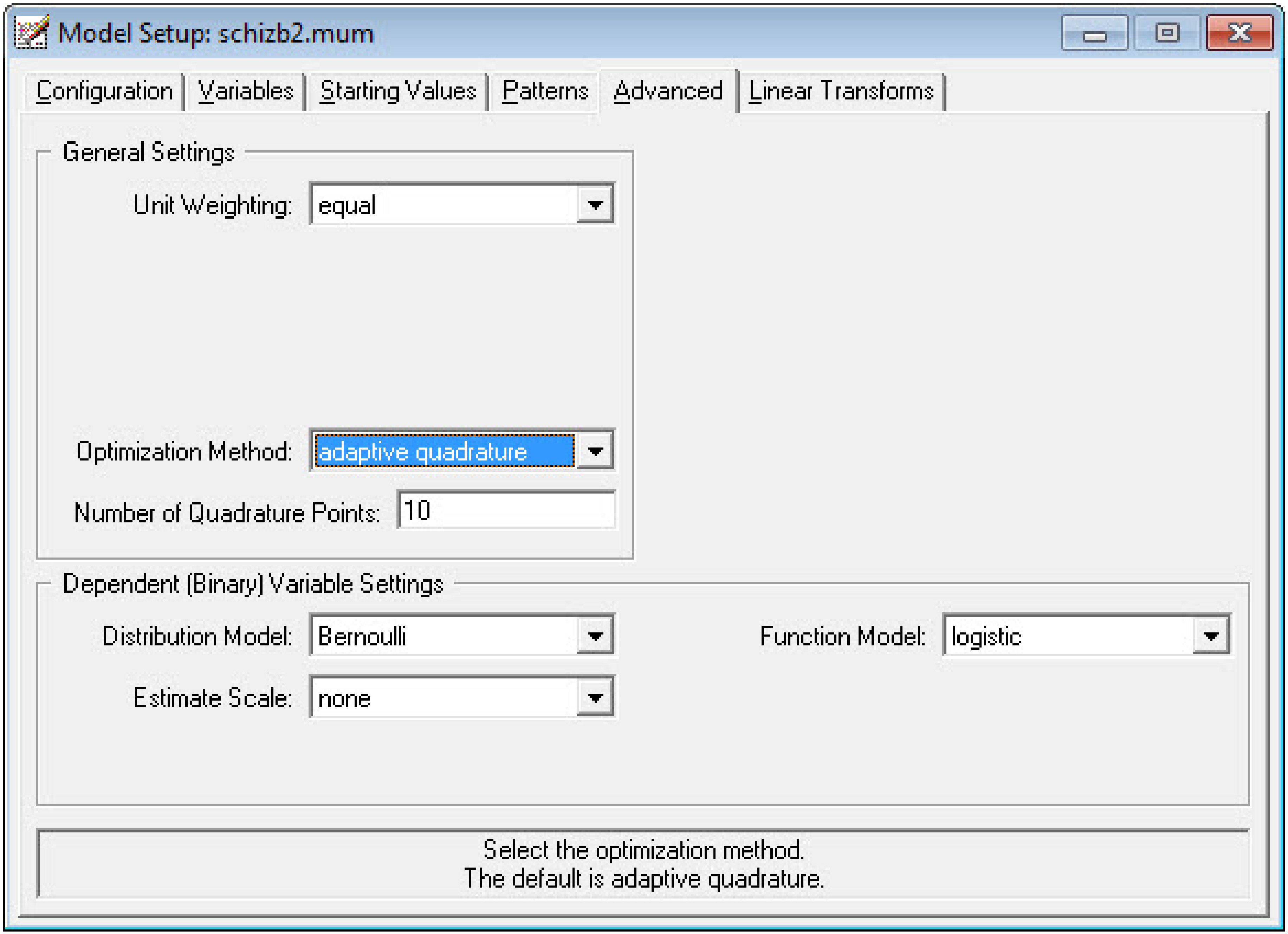
Note “Dependent Variable Type” should be “binary”



SqrtWeek is a level-2 (subject) random effect



Note "Optimization Method" should be "adaptive quadrature"



schizb2.out

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

Number of quadrature points =             10
Number of free parameters =                7
Number of iterations used =               11

-2lnL (deviance statistic) =       1227.75643
Akaike Information Criterion       1241.75643
Schwarz Criterion                  1279.41385
```

Estimated regression weights

Parameter	Estimate	Standard Error	z Value	P Value
intercept	5.9658	1.0030	5.9481	0.0000
TxDrug	0.3198	0.7561	0.4229	0.6723
Tx*SWeek	-1.6817	0.4972	-3.3821	0.0007
SqrtWeek	-1.3768	0.4974	-2.7681	0.0056

Odds Ratio and 95% Odds Ratio Confidence Intervals

Parameter	Estimate	Odds Ratio	Bounds Lower	Bounds Upper
intercept	5.9658	389.8732	54.5965	2784.0805
TxDrug	0.3198	1.3768	0.3128	6.0600
Tx*SWeek	-1.6817	0.1861	0.0702	0.4931
SqrtWeek	-1.3768	0.2524	0.0952	0.6690

Estimated level 2 variances and covariances

Parameter	Estimate	Standard Error	z Value	P Value
intercept/intercept	7.1851	3.1542	2.2780	0.0227
SqrtWeek/intercept	-2.2035	1.3003	-1.6945	0.0902
SqrtWeek/SqrtWeek	3.2386	1.2324	2.6279	0.0086

Save As... Close

$\Rightarrow$ Comparing models: $H0 : \sigma^2_{\upsilon_1} = \sigma_{\upsilon_{01}} = 0; \quad \chi^2_2 = 1249.73 - 1227.76 = 21.97, p < .001$

```
schizb2.out

                  intercept      SqrtWeek

intercept          7.185117
SqrtWeek          -2.203484      3.238562


Level 2 correlation matrix


                  intercept      SqrtWeek

intercept          1.000000
SqrtWeek          -0.456790      1.000000


                     Population Average Estimates

                                                Standard
 Parameter               Estimate                Error        z Value      P Value
 ---------               --------                --------     -------      -------
 intercept                 3.4632                  0.4745      7.2979       0.0000
 TxDrug                    0.0472                  0.5375      0.0879       0.9300
 Tx*SWeek                 -0.6609                  0.2867     -2.3055       0.0211
 SqrtWeek                 -0.9955                  0.2559     -3.8904       0.0001


     Odds Ratio and 95% Odds Ratio Confidence Intervals

                                                                    Bounds
 Parameter               Estimate              Odds Ratio      Lower        Upper
 ---------               --------              ----------      -----        -----
 intercept                 3.4632                 31.9181     12.5921      80.9052
 TxDrug                    0.0472                  1.0484      0.3656       3.0067
 Tx*SWeek                 -0.6609                  0.5164      0.2944       0.9057
 SqrtWeek                 -0.9955                  0.3696      0.2238       0.6102


  o=================================o
  | SuperMix used 1.11 seconds CPU |
  o=================================o

Save As...   Close
```

⇒ Supermix is FAST for a full-likelihood solution using bivariate numerical integration involving 100 quadrature points!

Empirical Bayes Estimates of Random Effects

Select “Analysis” > “View Level-2 Bayes Results”

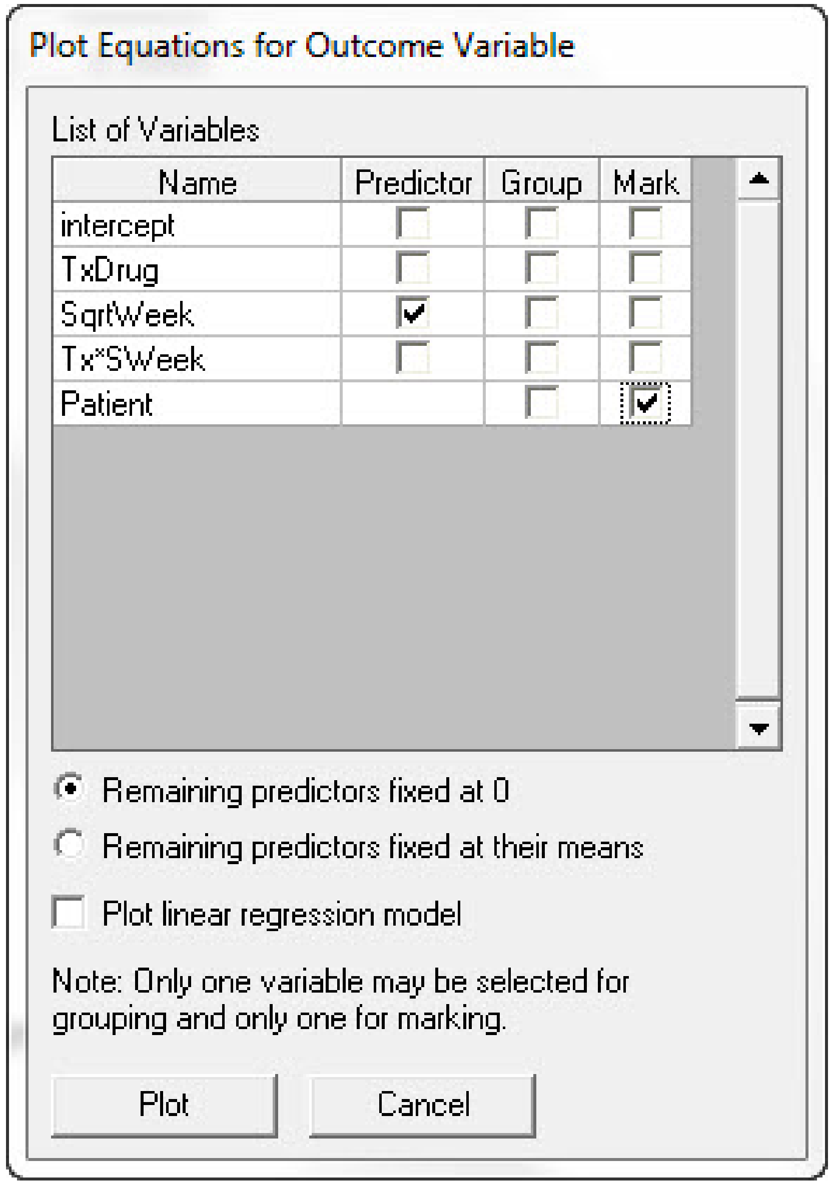
schizb2.ba2

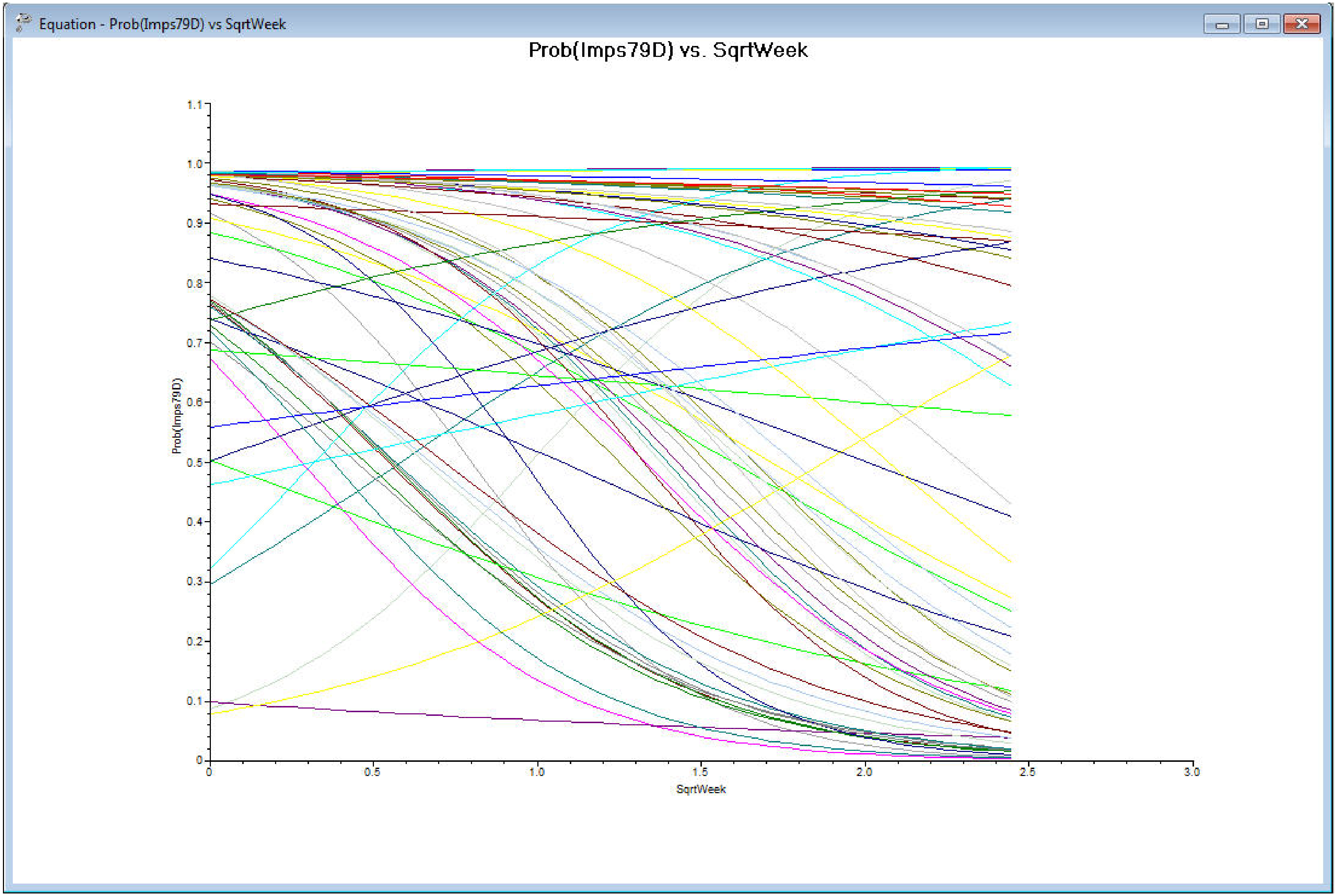
1103.00	1	-3.2254976	3.7395741	intercept
1103.00	2	1.2792848	1.4021073	SqrtWeek
1104.00	1	-2.2736372	4.1349330	intercept
1104.00	2	-1.1217700	2.3578041	SqrtWeek
1105.00	1	-2.3041210	4.1508661	intercept
1105.00	2	-1.0449592	2.5057265	SqrtWeek
1106.00	1	-5.6755917	2.9080543	intercept
1106.00	2	0.5967187	1.9782031	SqrtWeek
1107.00	1	0.4686978	6.2540200	intercept
1107.00	2	0.5867829	2.3490230	SqrtWeek
1108.00	1	0.7145179	6.2763860	intercept
1108.00	2	1.2879341	1.9980584	SqrtWeek
1109.00	1	-2.2736372	4.1349330	intercept
1109.00	2	-1.1217700	2.3578041	SqrtWeek
1110.00	1	0.7145179	6.2763860	intercept
1110.00	2	1.2879341	1.9980584	SqrtWeek
1111.00	1	0.9105483	5.7331291	intercept
1111.00	2	-0.4895328	1.7508380	SqrtWeek
1112.00	1	-1.4244996	5.3392174	intercept
1112.00	2	-0.2818097	1.5569574	SqrtWeek
1113.00	1	-1.7950498	4.4452986	intercept
1113.00	2	0.1649245	1.7232928	SqrtWeek
1114.00	1	0.9105483	5.7331291	intercept
1114.00	2	-0.4895328	1.7508380	SqrtWeek
1115.00	1	0.4686978	6.2540200	intercept
1115.00	2	0.5867829	2.3490230	SqrtWeek
1118.00	1	0.4951364	5.9589063	intercept
1118.00	2	0.0586369	3.1455239	SqrtWeek
1119.00	1	0.8682294	5.9061087	intercept
1119.00	2	-0.4698596	1.7886167	SqrtWeek

Save As... Close

ID, random effect number, estimate, variance, name

Close output, select “File” > “Model-based Graphs” > “Equations”




Equation - Prob(Imps79D) vs SqrtWeek
Prob(Imps79D) vs. SqrtWeek
Prob(Imps79D)
SqrtWeek
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
0.5
1.0
1.5
2.0
2.5
3.0

Summary - mixed models for binary outcomes

- link functions: logistic, probit, log-log, complementary log-log
- multiple random effects (correlated or independent) for up to 3-level models
- fast full-likelihood estimation using adaptive Gauss-Hermite quadrature
- subject-specific and population-average estimates and inference
- discrete/grouped time survival analysis via person-period dataset
- Advanced > Level-2 (Co)variance Patterns > Unidimensional
  - varying ICC model for MZ/DZ twin pair data: create dummy variables MZ and DZ, specify both as random effects, select "Unidimensional"
  - Item-response theory (IRT) models: create indicator variables for items, specify all as random effects, select "Unidimensional"