Mixed Models for Longitudinal Binary Outcomes

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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.

Multilevel 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 (& non-proportional) hazards models

  www.ssicentral.com/images/pdfs/Survival_clust.pdf

Logistic Regression Model

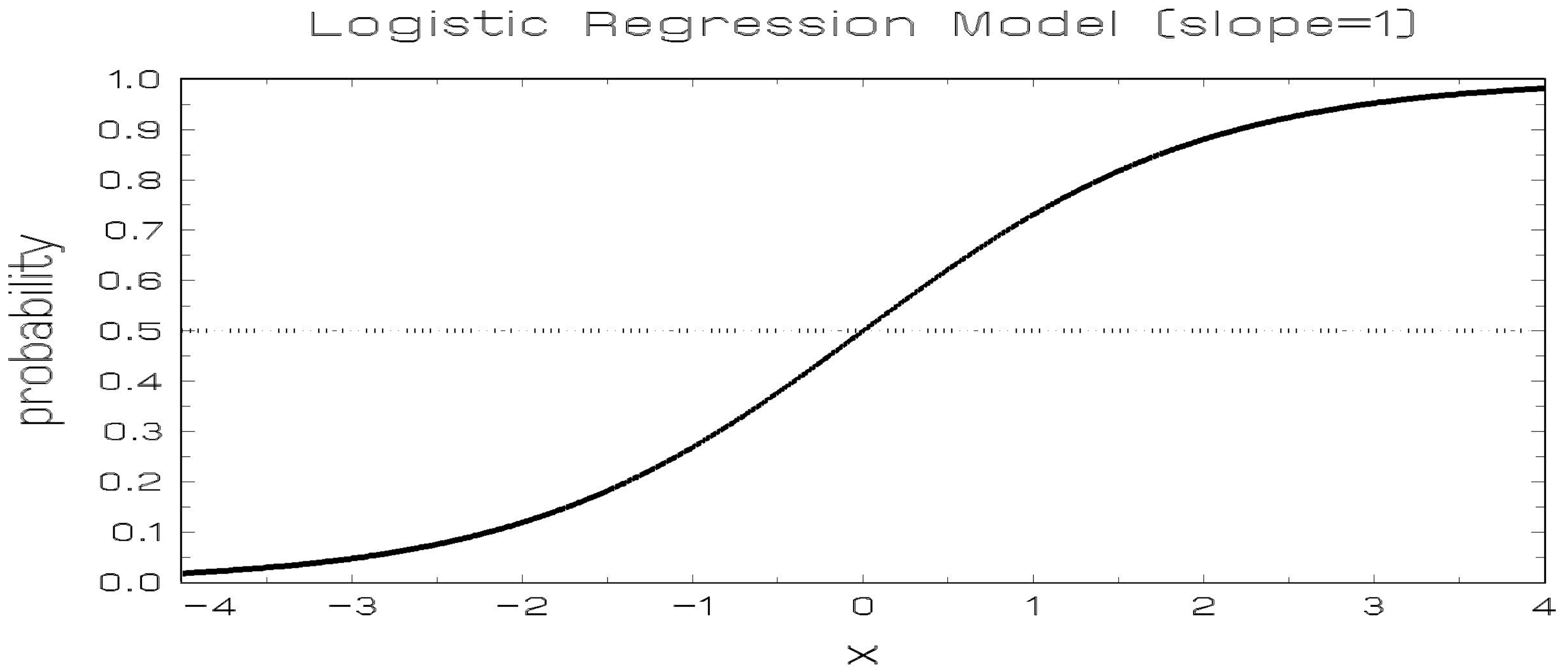
$$\log\left[\frac{P(Y_i = 1)}{1 - P(Y_i = 1)}\right] = \boldsymbol{x}_i'\boldsymbol{\beta}$$

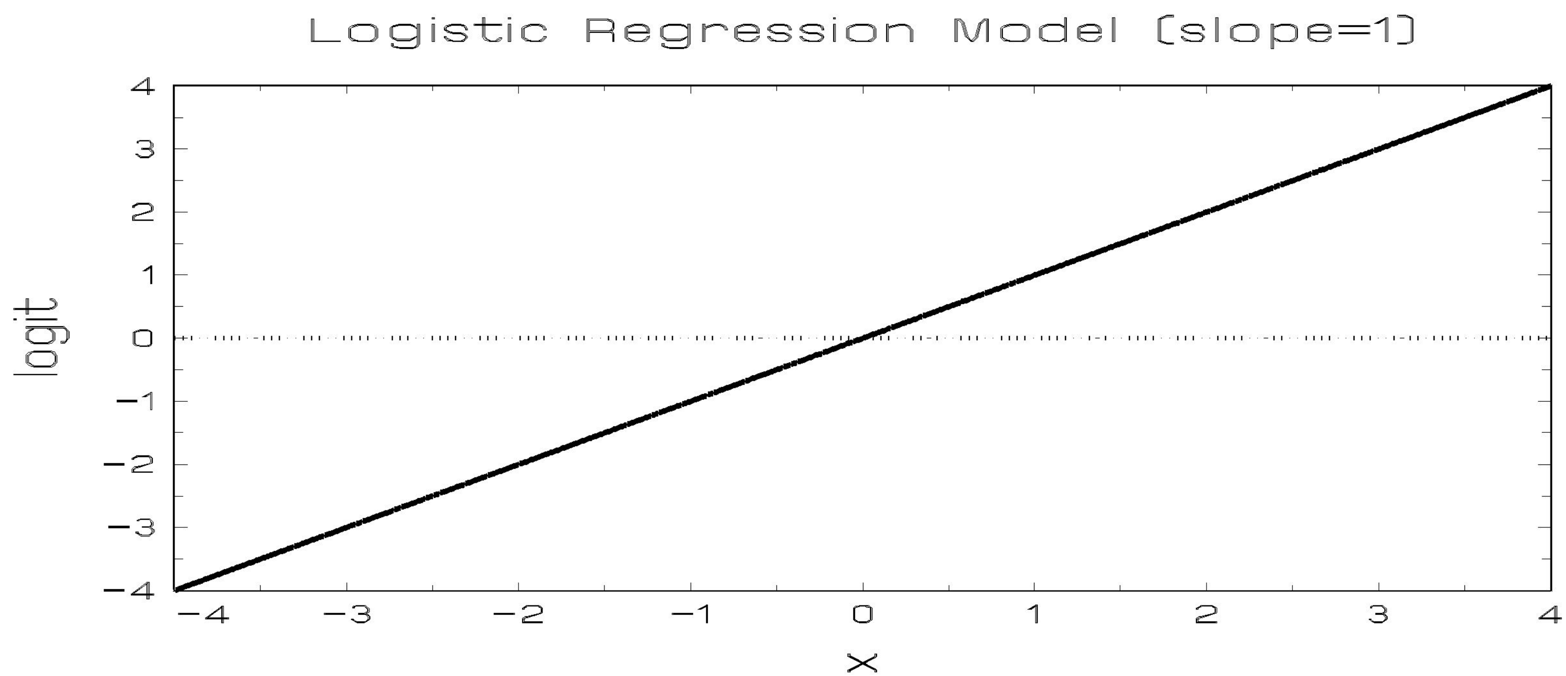
- Dichotomous outcome ($Y = 0$ absence, $Y = 1$ presence).
- Function that links probabilities to regressors is the logit (or log odds) function $\log[P/(1 - P]$. Logit is called the link function.

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.


Logistic Regression Model (slope=1)
probability
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
−4
−3
−2
−1
0
1
2
3
4
X


Logistic Regression Model (slope=1)
logit
4
3
2
1
0
−1
−2
−3
−4
−4
−3
−2
−1
0
1
2
3
4
X

The model can also be written in terms of the odds:

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

$\exp \beta =$ change in odds for Y per unit change of x

- $\beta = 0$ yields no effect on the odds
- $\beta > 0$ increases odds Y is present with increasing x
- $\beta < 0$ decreases odds Y is present with increasing x

Logistic Regression Model with dichotomous x

		Y = response				
group	x	0	1	prob	odds	logit
control	0	60	30	1/3	1/2	-.693
treatment	1	30	60	2/3	2	.693

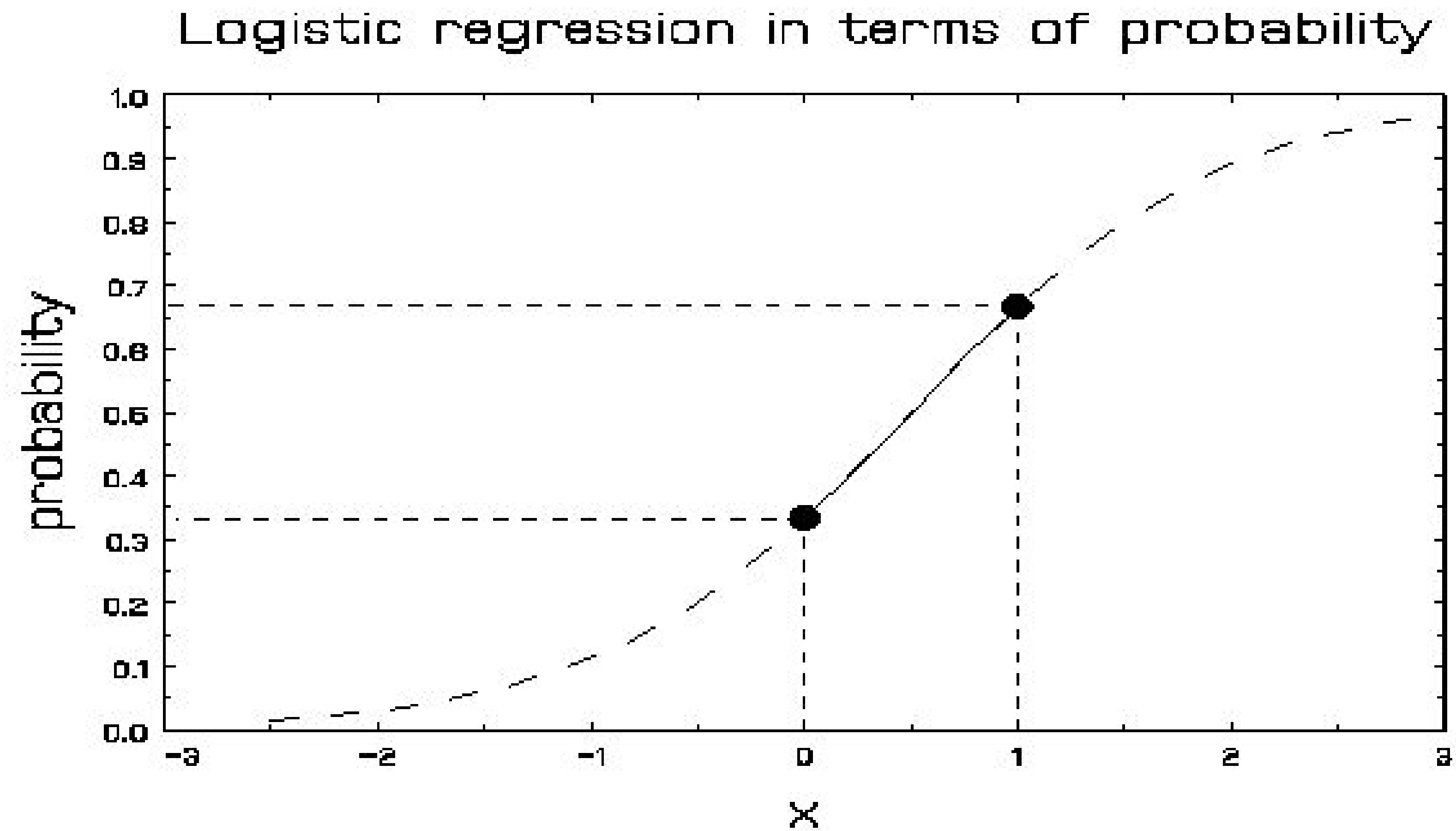
$$\log\left[\frac{Pr(Y_i = 1)}{1 - Pr(Y_i = 1)}\right] = \beta_0 + \beta_1 x_i$$

$$\begin{aligned} \exp\beta_0 &= \text{odds of response for } x = 0 \quad (30/60 = 1/2) \\ &\hat{\beta}_0 = \log(1/2) = -.693 \end{aligned}$$

$$\begin{aligned} \exp(\beta_0 + \beta_1) &= \text{odds of response for } x = 1 \quad (60/30 = 2) \\ &\hat{\beta}_0 + \hat{\beta}_1 = \log(2) = .693 \\ &\hat{\beta}_1 = .693 + .693 = 1.386 \end{aligned}$$

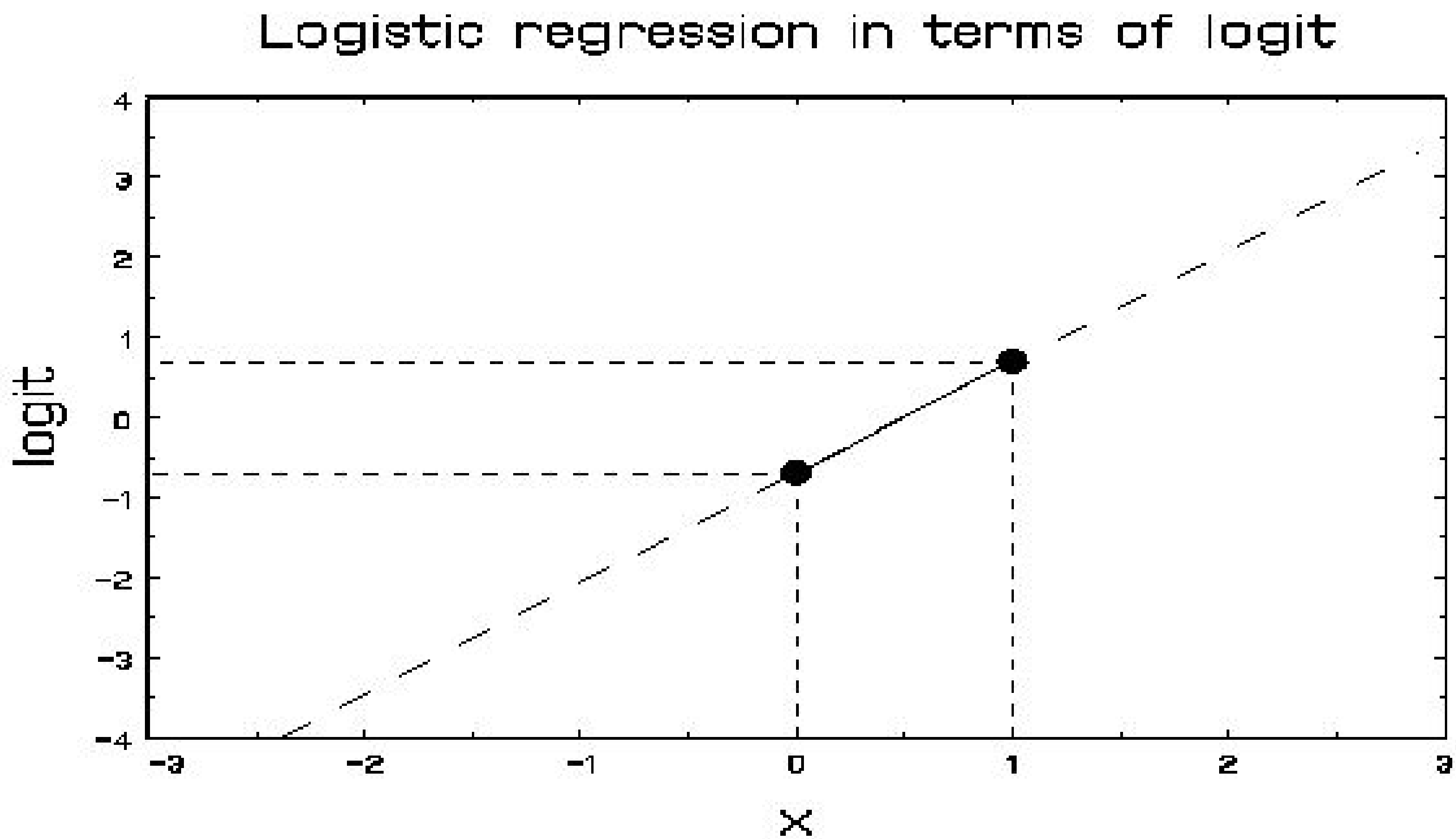
$$
\begin{aligned}
\text{odds ratio} &= \text{ratio of odds per unit change in } x \\
&= \frac{\exp(\hat{\beta}_0 + \hat{\beta}_1)}{\exp(\hat{\beta}_0)} \\
&= \exp(\hat{\beta}_1) \\
&= \exp(1.386) = 4
\end{aligned}
$$

Model is not linear in terms of the probabilities



$$Pr(Y_i = 1) = \frac{1}{1 + \exp[-(\beta_0 + \beta_1 x_i)]} = \frac{\exp(\beta_0 + \beta_1 x_i)}{1 + \exp(\beta_0 + \beta_1 x_i)}$$

Model is linear in terms of the logits



$$\log\left[\frac{Pr(Y_i=1)}{1-Pr(Y_i=1)}\right] = \beta_0 + \beta_1 x_i$$

Logistic Regression Model with continuous x

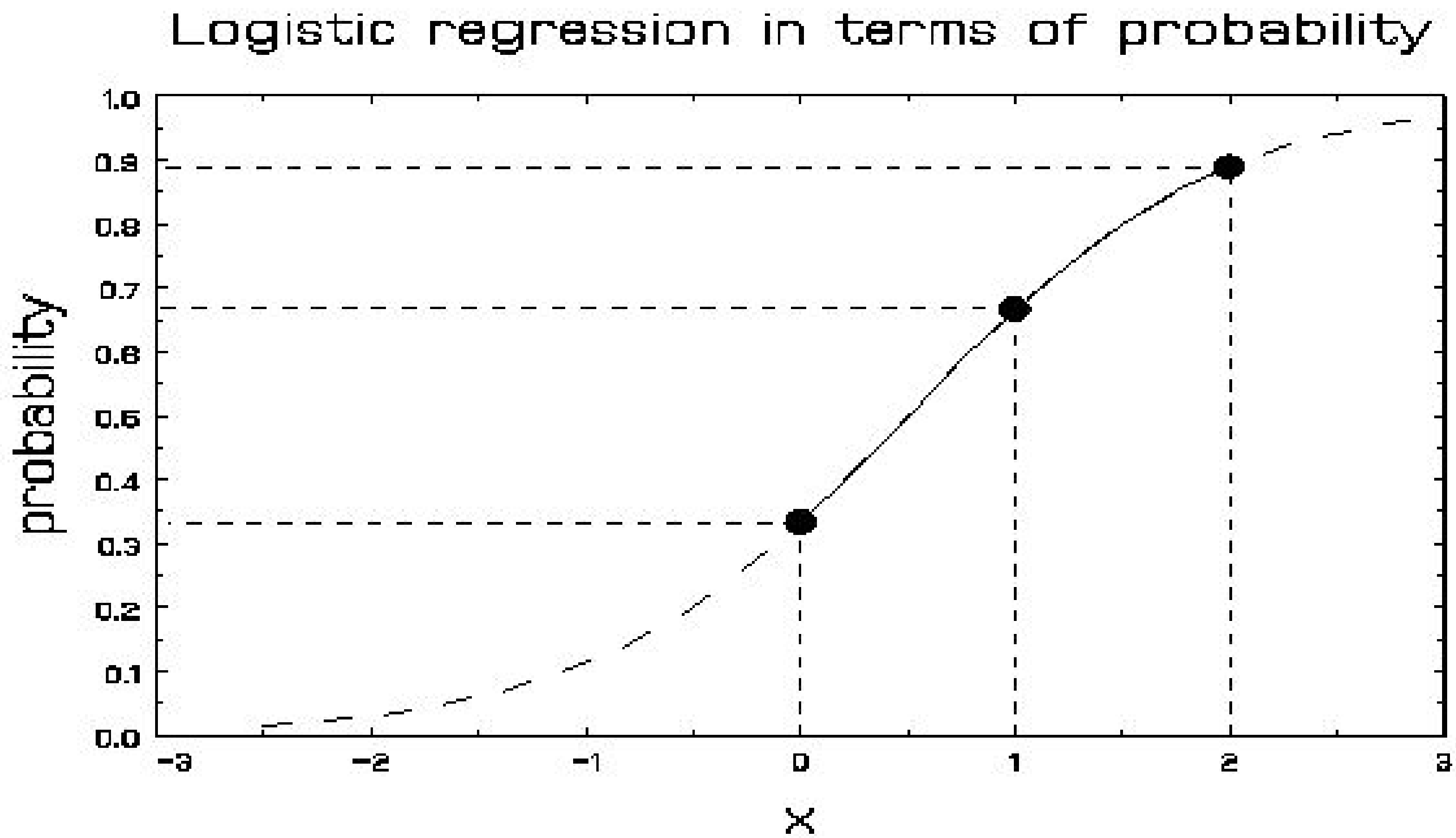
		Y = response				
age	x	0	1	prob	odds	logit
20-29	0	60	30	1/3	1/2	-.693
30-39	1	30	60	2/3	2	.693
40-49	2	10	80	8/9	8	2.079

$$\log\left[\frac{Pr(Y_i = 1)}{1 - Pr(Y_i = 1)}\right] = \beta_0 + \beta_1 x_i$$

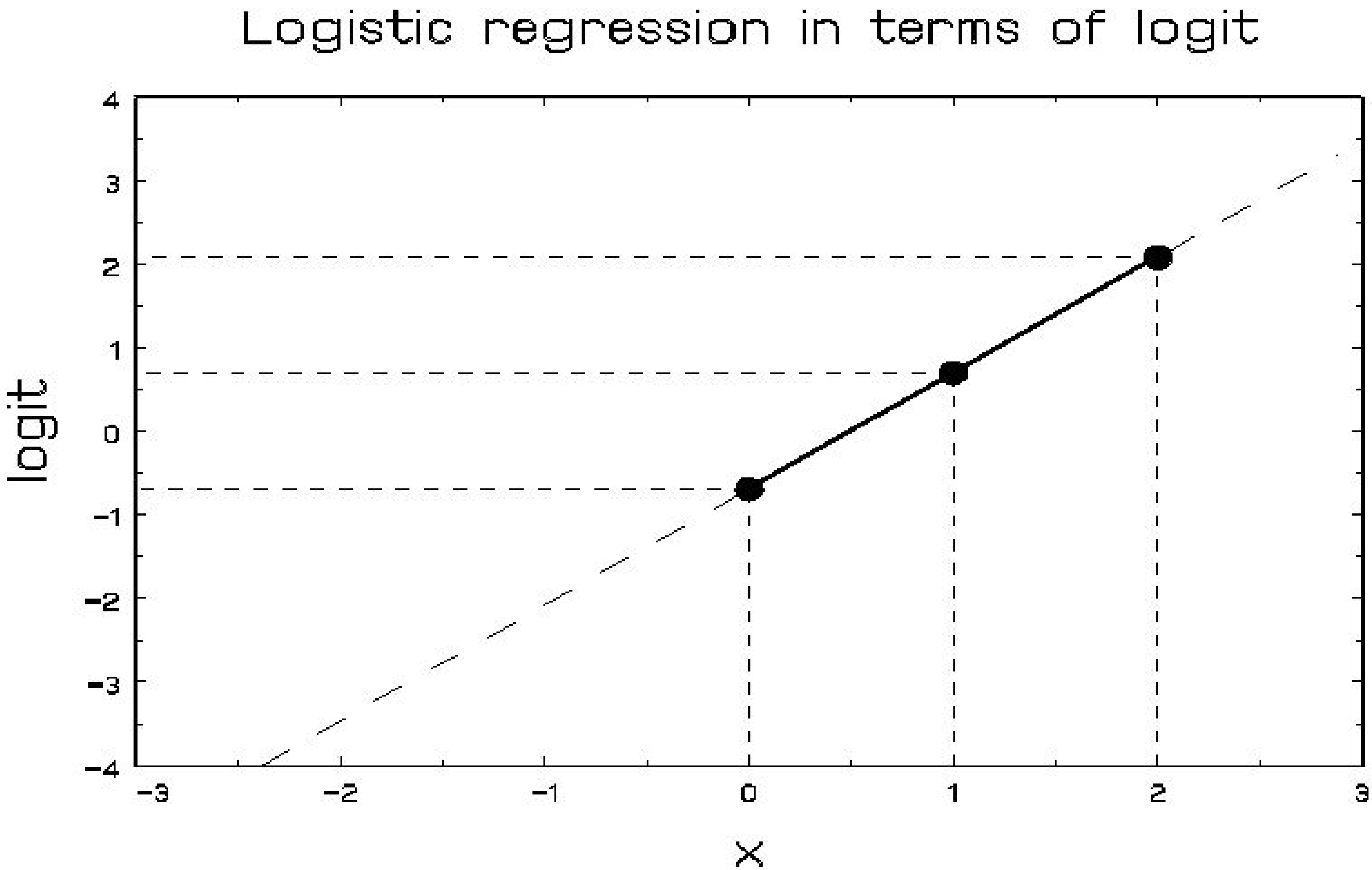
$$\hat{\beta}_0 = -.693$$

$$\begin{aligned}\hat{\beta}_1 &= \text{change in log odds w/ unit change in } x \\ &= 1.386\end{aligned}$$

$$
\begin{aligned}
\text{odds ratio} &= \text{ratio of odds per unit change in } x \\
&= \exp(\hat{\beta}_1) \\
&= \exp(1.386) = 4
\end{aligned}
$$



$$Pr(Y_i = 1) = \frac{1}{1 + \exp[-(\beta_0 + \beta_1 x_i)]} = \frac{\exp(\beta_0 + \beta_1 x_i)}{1 + \exp(\beta_0 + \beta_1 x_i)}$$

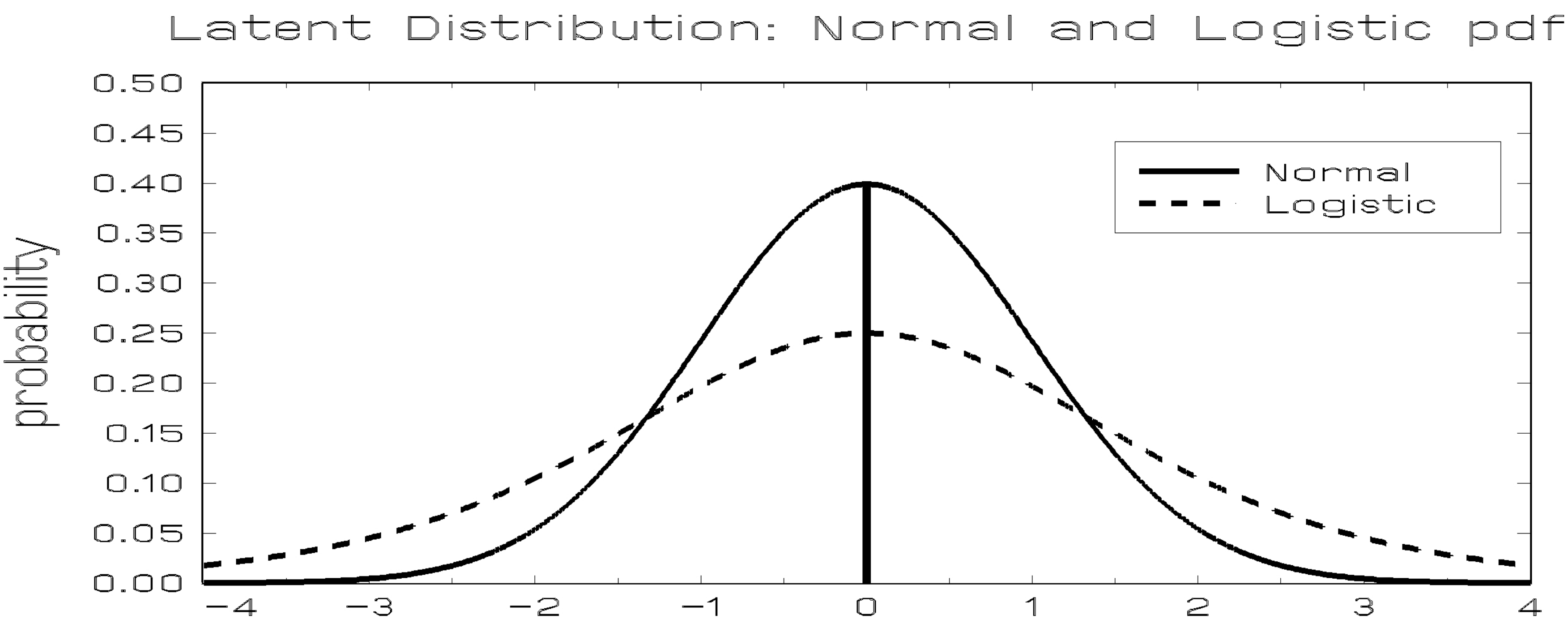


$$\log\left[\frac{Pr(Y_i = 1)}{1 - Pr(Y_i = 1)}\right] = \beta_0 + \beta_1 x_i$$

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 ($j = 1, 2, \ldots, n_i$):

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

where

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

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

In clustered case, σ_υ^2 is usually relatively small and the difference in size of $\boldsymbol{\beta}$ estimates is also small. However, for longitudinal data, σ_υ^2 is usually relatively large and the difference in size of $\boldsymbol{\beta}$ estimates is therefore much larger.

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?

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

Stata code: schizb_plots.do

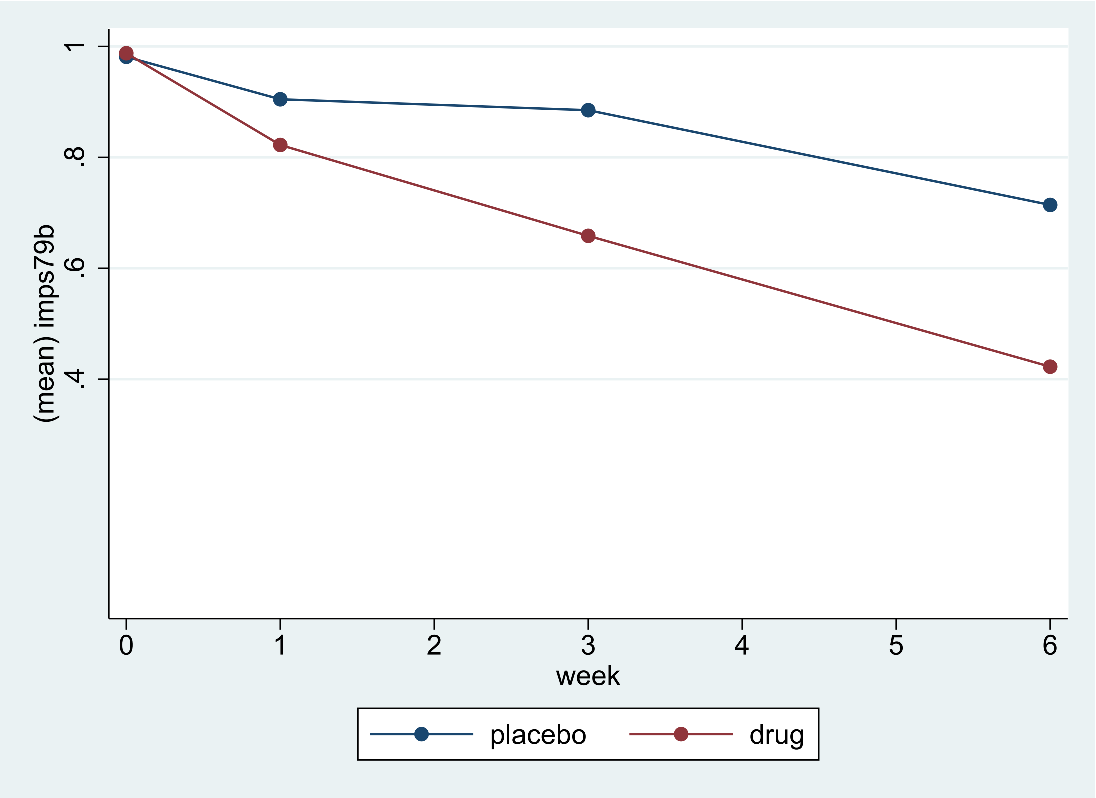
```
log using U:\Data\StatHorizons\schizb_plots.log, replace
infile  id imps79 imps79b imps79o inter tx week sweek txswk ///
using https://hedeker.people.uic.edu/SCHIZX1.DAT.txt, clear
recode imps79 imps79b imps79o (-9=.)

/* only use weeks 0, 1, 3, 6 for these descriptives */
keep if week == 0 | week == 1 | week == 3 | week == 6
summarize
collapse (mean) p1=imps79b, by (tx week)
gen odds1 = p1 / (1-p1)
gen logit1 = log(odds1)
list tx week p1 odds1 logit1

* graph probabilities & logits
graph twoway (connected p1 week if tx==0) ///
             (connected p1 week if tx==1), ///
             legend(label(1 "placebo") label(2 "drug")) ///
             yscale(range(0 1)) xlabel(0(1)6)
graph twoway (connected logit1 week if tx==0) ///
             (connected logit1 week if tx==1), ///
             legend(label(1 "placebo") label(2 "drug")) ///
             yscale(range(-0.5 4.5)) xlabel(0(1)6)
```

```
gen srweek = sqrt(week)
graph twoway (connected logit1 srweek if tx==0) ///
             (connected logit1 srweek if tx==1), ///
             legend(label(1 "placebo") label(2 "drug")) ///
             yscale(range(-0.5 4.5)) xlabel(0(.5)2.5)
```

```
. collapse (mean) p1=imps79b, by (tx week)
. gen odds1 = p1 / (1-p1)
. gen logit1 = log(odds1)
. list tx week p1 odds1 logit1

     +----------------------------------------------+
     | tx   week         p1      odds1      logit1  |
     |----------------------------------------------|
  1. |  0      0   .9813084   52.49997   3.960813  |
  2. |  0      1   .9047619   9.500001   2.251292  |
  3. |  0      3   .8850574   7.699998    2.04122  |
  4. |  0      6   .7142857        2.5   .9162908  |
     |----------------------------------------------|
  5. |  1      0   .9877676   80.74995   4.391357  |
  6. |  1      1   .8224299   4.631578   1.532898  |
  7. |  1      3   .6585366   1.928572   .6567797  |
  8. |  1      6   .4226415   .7320262   -.311939  |
     +----------------------------------------------+
```

Observed Proportions across Time by Condition

```
. graph twoway (connected p1 week if tx==0) ///
>              (connected p1 week if tx==1), ///
>                          legend(label(1 "placebo") label(2 "drug")) ///
>                          yscale(range(0 1)) xlabel(0(1)6)
```

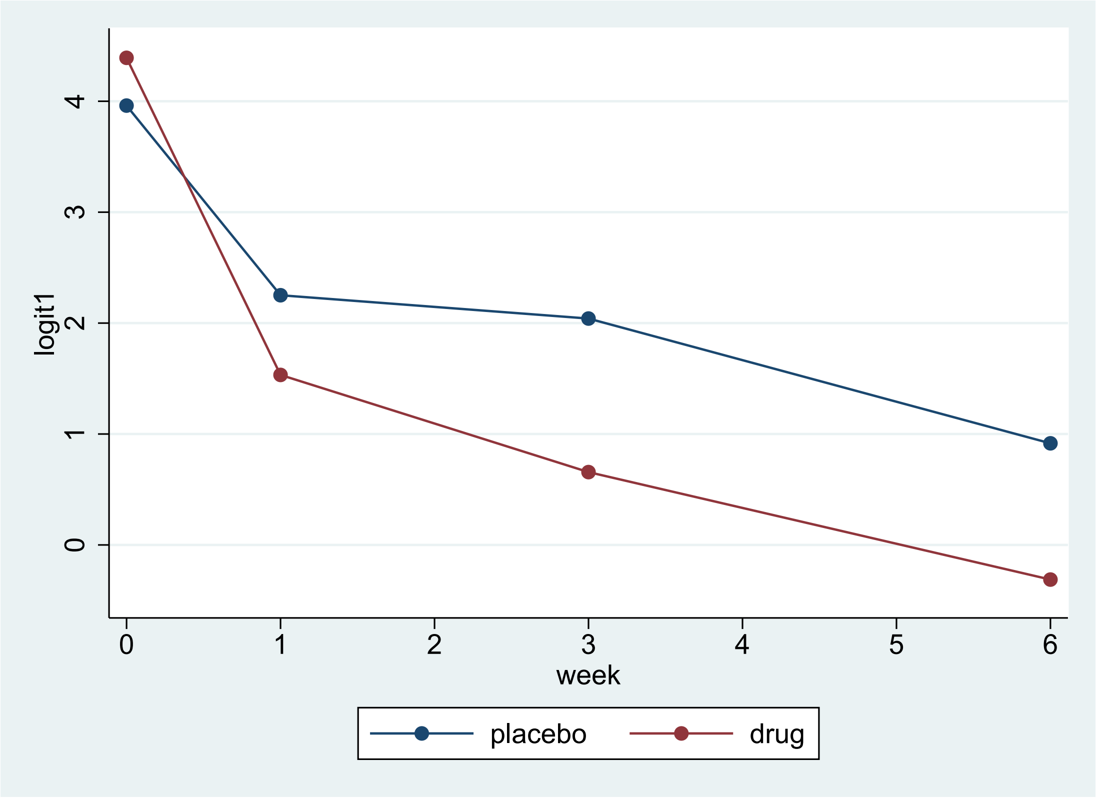


- model is not linear in terms of probabilities

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

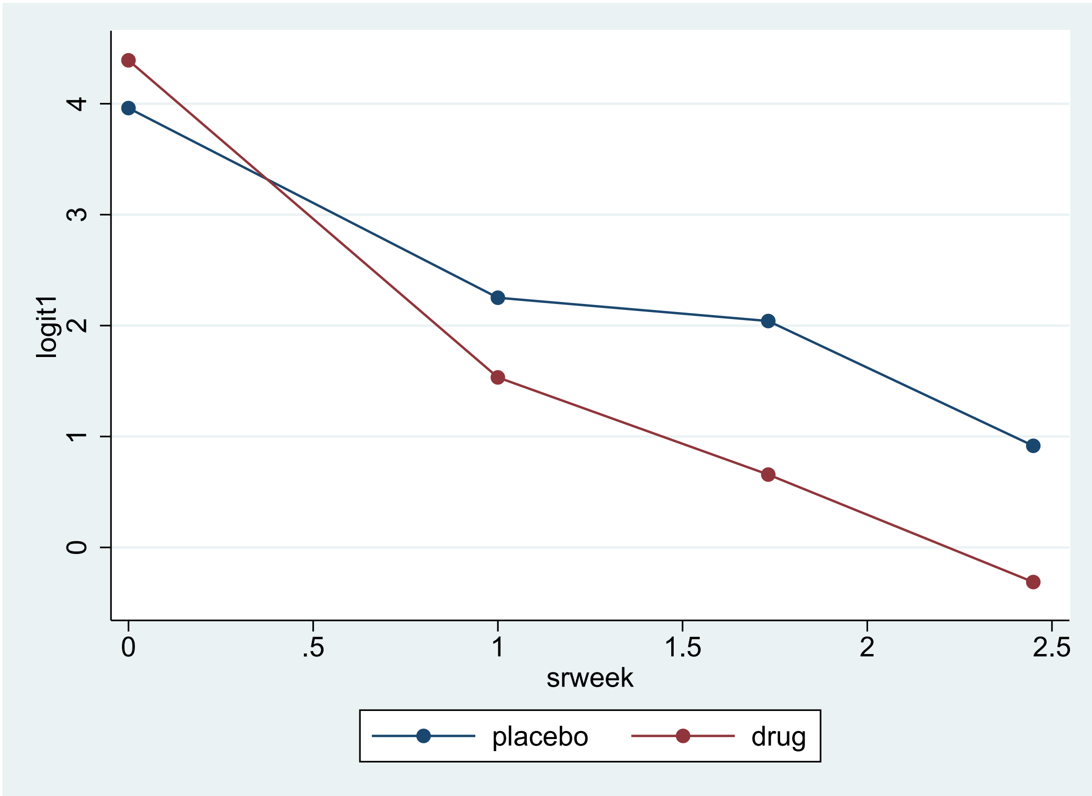
Observed Logits across Time by Condition

```
. graph twoway (connected logit1 week if tx==0) ///
>              (connected logit1 week if tx==1), ///
>                          legend(label(1 "placebo") label(2 "drug")) ///
>                          yscale(range(-0.5 4.5)) xlabel(0(1)6)
```



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

```
. gen srweek = sqrt(week)
. graph twoway (connected logit1 srweek if tx==0) ///
>              (connected logit1 srweek if tx==1), ///
>                          legend(label(1 "placebo") label(2 "drug")) ///
>                          yscale(range(-0.5 4.5)) xlabel(0(.5)2.5)
```



$\Rightarrow$ time effect is approximately linear when expressed as $\sqrt{week}$

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* $\quad (i = 1, \ldots, N \text{ subjects})$

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

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

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

Put together,

$$logit_{ij} = (\beta_0 \; + \; \beta_2 Grp_i \; + \; \upsilon_{0i}) \; + \; (\beta_1 \; + \; \beta_3 Grp_i)\sqrt{Week}_j$$

Stata code: `schizb.do`

```
log using c:\Stata_Examples\schizb.log, replace
infile  id imps79 imps79b imps79o inter tx week sweek txswk ///
using https://hedeker.people.uic.edu/SCHIZX1.DAT.txt, clear
recode imps79 imps79b imps79o (-9=.)
summarize

* random intercept model
melogit imps79b sweek tx txswk || id:
scalar m1 = e(ll)

* random intercept and trend model
melogit imps79b sweek tx txswk || id:sweek,covariance(unstructured)
scalar m2 = e(ll)

* obtain the random effects for each subject
predict u1 u0, reffects

* list the random effects for the first few subjects
by id, sort: generate tolist = (_n==1)
list id u0 u1 in 1/30 if tolist
```

```
* add random and fixed effects together, list out a few
generate intercept = _b[_cons] + _b[tx]*tx + u0
generate slope = _b[sweek] + _b[txswk]*tx + u1
list id intercept slope in 1/30 if tolist

* plot subjects intercepts and slopes
local yref = _b[_cons]
local xref = _b[sweek]
twoway scatter intercept slope, yline(`yref', lpattern(dash)) ///
       xline(`xref', lpattern(dash))

* generate an estimated spaghetti plot
predict fitimps79b, fitted
sort id sweek
twoway connected fitimps79b sweek, connect(L)

* get LR test for comparing models
display "chibar(12) = " 2*(m2-m1)
display "Prob > chibar2(12) = " .5*chi2tail(1, 2*(m2-m1)) + ///
        .5*chi2tail(2, 2*(m2-m1))
log close
```

```
. summarize

    Variable |        Obs        Mean    Std. Dev.       Min        Max
-------------+---------------------------------------------------------
          id |      3,059    4777.735    2438.694       1103       9316
      imps79 |      1,603    4.373051    1.471493          1          7
     imps79b |      1,603    .7679351    .4222819          0          1
     imps79o |      1,603    2.796007    1.028403          1          4
       inter |      3,059           1           0          1          1
-------------+---------------------------------------------------------
          tx |      3,059    .7528604    .4314191          0          1
        week |      3,059           3    2.000327          0          6
       sweek |      3,059    1.547414    .7783017          0     2.4495
       txswk |      3,059    1.164987    .9495875          0     2.4495
```

```
Mixed-effects logistic regression               Number of obs     =      1,603
Group variable:             id                  Number of groups  =        437

                                                Obs per group:
                                                              min =          2
                                                              avg =        3.7
                                                              max =          5

Integration method: mvaghermite                 Integration pts.  =          7
                                                Wald chi2(3)      =     170.73
Log likelihood = -624.82526                     Prob > chi2       =     0.0000
------------------------------------------------------------------------------
     imps79b |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       sweek |  -1.498166   .2899992    -5.17   0.000    -2.066554   -.9297781
          tx |  -.0131162   .6548128    -0.02   0.984    -1.296526    1.270293
       txswk |  -1.019937   .3345059    -3.05   0.002    -1.675556   -.3643169
       _cons |   5.383934   .6299046     8.55   0.000     4.149344    6.618524
-------------+----------------------------------------------------------------
id           |
   var(_cons)|   4.506713   .9568774                      2.972559    6.832652
------------------------------------------------------------------------------
LR test vs. logistic model: chibar2(01) = 112.41      Prob >= chibar2 = 0.0000
```

Intraclass Correlation (ICC)

$$ICC = \frac{4.507}{4.507 + \pi^2/3} = 0.578$$

- average pairwise correlation of repeated outcomes = .58
- proportion of (unexplained) variation at the subject level is 58%

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* $\quad (i = 1, \ldots, N \text{ subjects})$

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

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

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

Put together,

$$logit_{ij} = (\beta_0 \; + \; \beta_2 Grp_i \; + \; \upsilon_{0i}) \; + \; (\beta_1 \; + \; \beta_3 Grp_i \; + \; \upsilon_{1i})\sqrt{Week}_j$$

```
. melogit imps79b sweek tx txswk || id: sweek, covariance(unstructured)


Mixed-effects logistic regression               Number of obs     =      1,603
Group variable:              id                 Number of groups  =        437

                                                Obs per group:
                                                              min =          2
                                                              avg =        3.7
                                                              max =          5

Integration method: mvaghermite                 Integration pts.  =          7

                                                Wald chi2(3)      =      60.20
Log likelihood = -613.70418                     Prob > chi2       =     0.0000
------------------------------------------------------------------------------
     imps79b |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
       sweek |  -1.429712   .4965533    -2.88   0.004    -2.402939   -.4564858
          tx |   .2873997   .7558803     0.38   0.704    -1.194098    1.768898
       txswk |  -1.608433   .4879325    -3.30   0.001    -2.564763   -.6521025
       _cons |   5.974928   .9836365     6.07   0.000     4.047036    7.902821
-------------+----------------------------------------------------------------
id           |
```

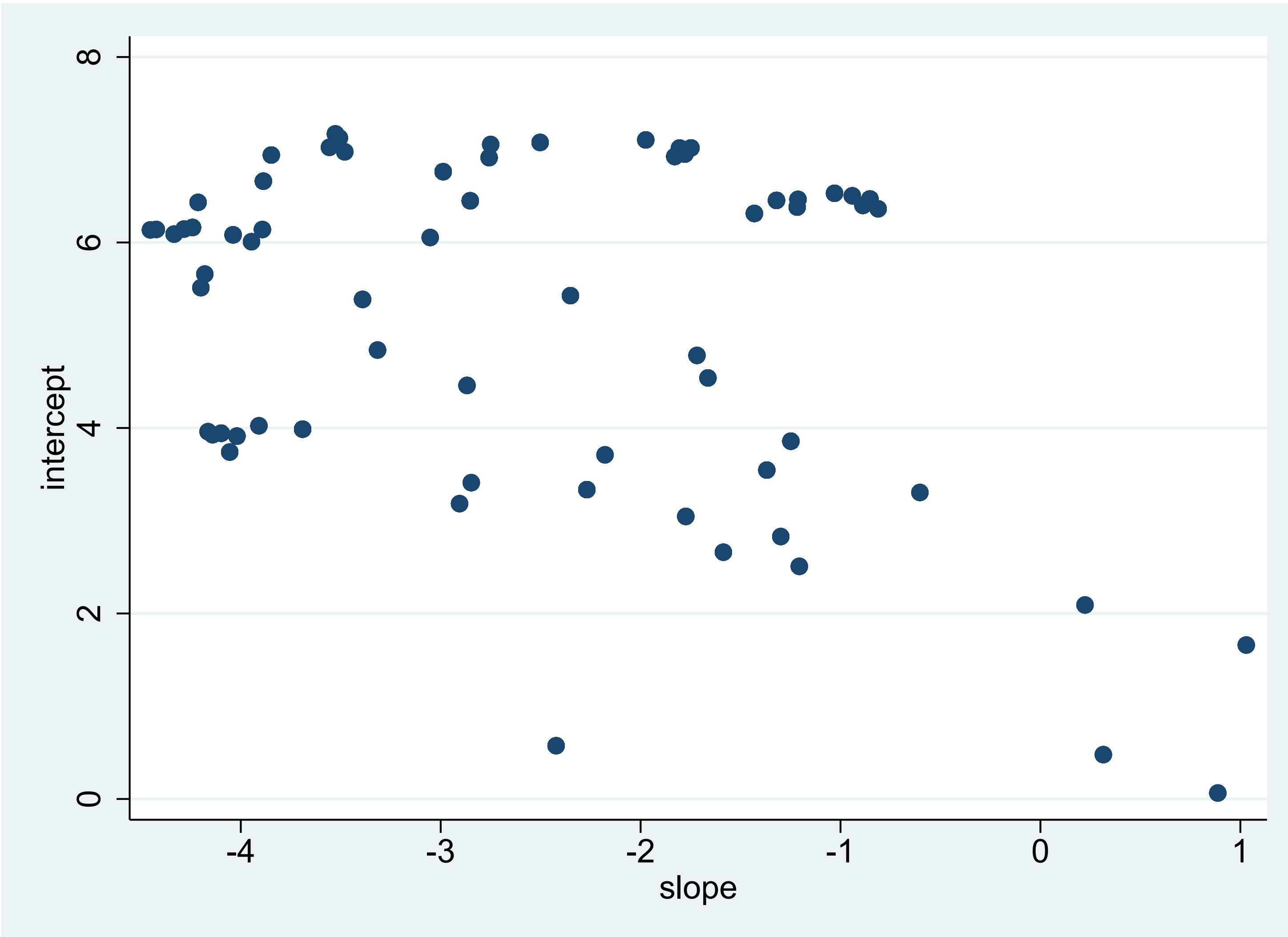
```
      var(sweek)|   3.093755   1.186109                      1.459303    6.558831
      var(_cons)|   7.226627   3.246852                      2.995706      17.433
----------------+--------------------------------------------------------------
id              |
cov(_cons,sweek)|  -2.172073   1.285726    -1.69   0.091     -4.69205    .3479036
-------------------------------------------------------------------------------
LR test vs. logistic model: chi2(3) = 134.66              Prob > chi2 = 0.0000

Note: LR test is conservative and provided only for reference.
```

Postestimation: `schizb.do`

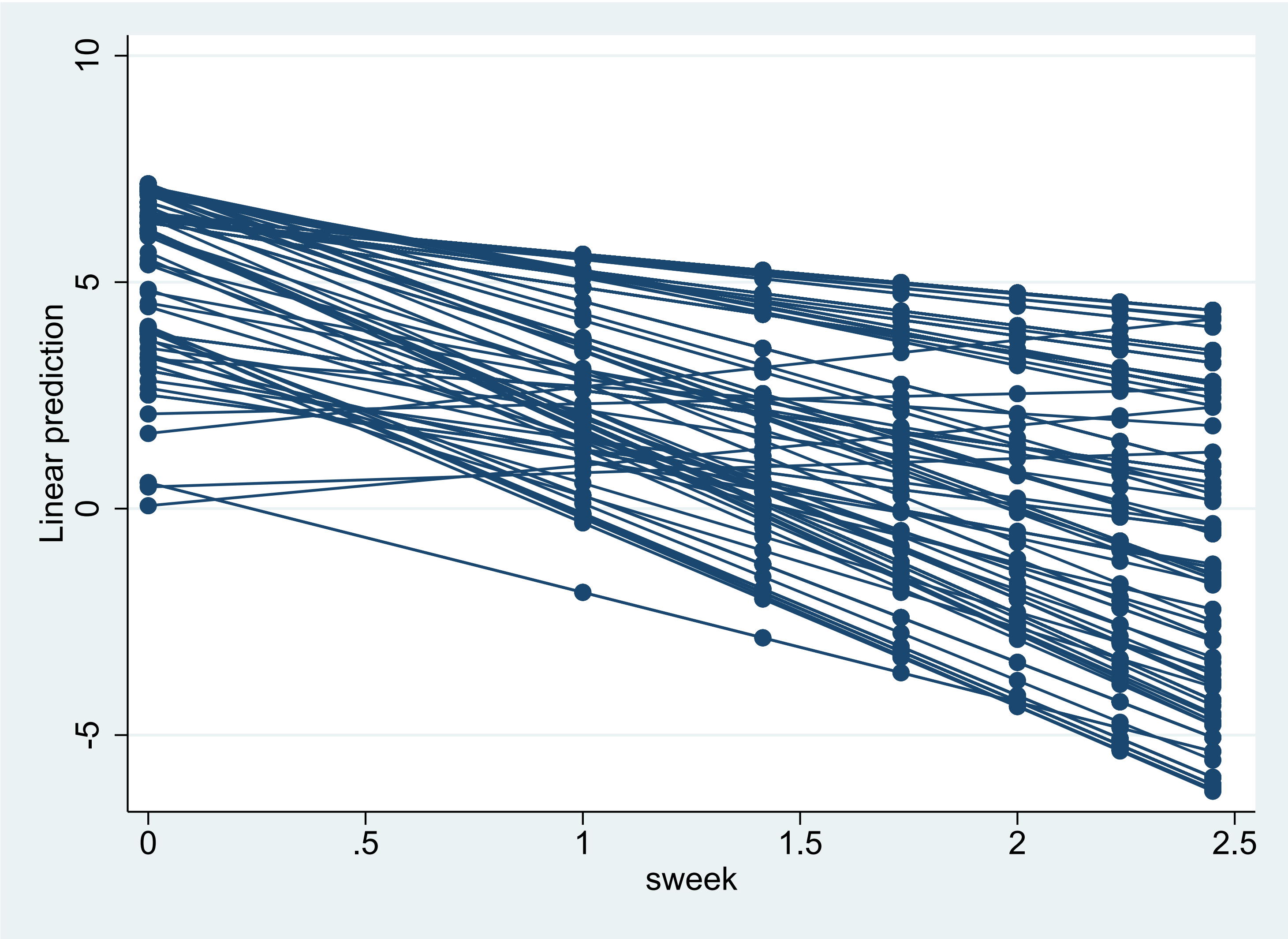
```
* obtain the random effects for each subject
predict u1 u0, reffects

* list the random effects for the first few subjects
by id, sort: generate tolist = (_n==1)
list id u0 u1 in 1/30 if tolist

     +-------------------------------+
     |   id          u0           u1 |
     |-------------------------------|
  1. | 1103   -3.215459     1.264197 |
  8. | 1104   -2.318756    -1.059744 |
 15. | 1105   -2.349588    -.9809698 |
 22. | 1106   -5.687785     .6155943 |
 29. | 1107    .4937801     .5770214 |
     +-------------------------------+
```

```
* add random and fixed effects together, list out a few
generate intercept = _b[_cons] + _b[tx]*tx + u0
generate slope = _b[sweek] + _b[txswk]*tx + u1
list id intercept slope in 1/30 if tolist

     +-----------------------------+
     |   id   interc~t       slope |
     |-----------------------------|
  1. | 1103   3.046869   -1.773948 |
  8. | 1104   3.943572   -4.097889 |
 15. | 1105    3.91274   -4.019115 |
 22. | 1106   .5745431   -2.422551 |
 29. | 1107   6.468709    -.852691 |
     +-----------------------------+
```

```
* plot subjects intercepts and slopes
local yref = _b[_cons]
local xref = _b[sweek]
twoway scatter intercept slope, yline(‘yref’, lpattern(dash)) ///
       xline(‘xref’, lpattern(dash))
```



```
* generate an estimated spaghetti plot
predict fitimps79b, fitted
sort id sweek
twoway connected fitimps79b sweek, connect(L)
```



Model comparisons - Likelihood Ratio (LR) tests

- comparing random intercept to ordinary logistic regression

  `LR test vs. logistic model: chibar2(01) = 112.41 Prob >= chibar2 = 0.0000`

  $H_0 : \sigma_\upsilon^2 = 0, \quad H_A : \sigma_\upsilon^2 > 0 \quad \Rightarrow$ one-sided test

  `chibar2(01)` refers to a 50:50 mixture of a χ_0^2 and a χ_1^2 distribution; chi-bar square distribution; p-value is obtained from χ_1^2, but is halved

- comparing random trend to ordinary logistic regression

  ```
  LR test vs. logistic model: chi2(3) = 134.66        Prob > chi2 = 0.0000
  Note: LR test is conservative and provided only for reference.
  ```

  $H_0 : \sigma_{\upsilon_0}^2 = \sigma_{\upsilon_1}^2 = \sigma_{\upsilon_{01}} = 0$

- comparing random trend to random intercept model

  $H_0 : \sigma^2_{\upsilon_1} = \sigma_{\upsilon_{01}} = 0$

  need **`chibar2(12)`**, 50:50 mixture of a χ^2_1 and a χ^2_2 distribution; p-value is obtained from the average of χ^2_1 and χ^2_2 (i.e., q and $q-1$, where q is the number of (co)variance parameters in the null)

```
. * get LR test for comparing models
. display "chibar(12) = " 2*(m2-m1)
chibar(12) = 22.242157

. display "Prob > chibar2(12) = " .5*chi2tail(1, 2*(m2-m1)) + ///
>          .5*chi2tail(2, 2*(m2-m1))
Prob > chibar2(12) = 8.600e-06
```

SAS for mixed model analysis of binary outcomes

PROC GLIMMIX (version 9.1.3 and thereafter)

- Multiple levels of nesting, crossed random effects
- Pseudo-likelihood estimation (by default)
  - Linearization to avoid integration over the random effects
  - Produces biased estimates if number of level-1 or level-2 units is small and/or ICC is large
- Full likelihood estimation using numerical quadrature for integration over the random effects `METHOD=QUAD`; however for 3-level models can only use `METHOD=QUAD(QPOINTS=1)` or `METHOD=LAPLACE` (these are equivalent)

PROC NLMIXED

- Full likelihood estimation using numerical quadrature for integration over the random effects
- Only for 2-level models; allows programming features
  (can do 3-level models with SAS/STAT 13.2; 2nd maintenance release for SAS 9.4)

SAS Example: `schizb.sas`

```
FILENAME SchizDat HTTP "https://hedeker.people.uic.edu/SCHIZX1.DAT.txt";
DATA  one; INFILE SchizDat;
INPUT id imps79 imps79b imps79o int tx week sweek txswk ;
```

sometimes doesn't seem to work ....

```
ERROR: The connection has timed out..
NOTE: The SAS System stopped processing this step because of errors.
```

in this case, easiest just to go to URL and download the data

```
FILENAME SchizDat  "U:/mixdemo/SCHIZX1.DAT.txt";
DATA  one; INFILE SchizDat;
INPUT id imps79 imps79b imps79o int tx week sweek txswk ;
```

SAS code: `schizb.sas`

```
FILENAME SchizDat HTTP "https://hedeker.people.uic.edu/SCHIZX1.DAT.txt";
DATA  one; INFILE SchizDat;
INPUT id imps79 imps79b imps79o int tx week sweek txswk ;

/* get rid of observations with missing values */
IF imps79 > -9;

/* random intercept logistic regression via GLIMMIX */
PROC GLIMMIX DATA=one METHOD=QUAD NOCLPRINT;
CLASS id;
MODEL imps79b(DESC) = tx sweek tx*sweek / SOLUTION DIST=BINARY LINK=LOGIT;
RANDOM INTERCEPT / SUBJECT=id;
COVTEST 'test of random intercept' GLM;
```

- `METHOD=QUAD` requests full-likelihood estimation (using numerical quadrature)
- `COVTEST 'test of random intercept' GLM;`
  statement yields a likelihood ratio test of
  $H_0 : \sigma^2_{\upsilon_0} = 0, \quad H_A : \sigma^2_{\upsilon_0} > 0 \quad \Rightarrow$ one-sided test

The SAS System

The GLIMMIX Procedure

Model Information

Data Set	WORK.ONE
Response Variable	imps79b
Response Distribution	Binary
Link Function	Logit
Variance Function	Default
Variance Matrix Blocked By	id
Estimation Technique	Maximum Likelihood
Likelihood Approximation	Gauss-Hermite Quadrature
Degrees of Freedom Method	Containment

Number of Observations Read	1603
Number of Observations Used	1603

Response Profile

Ordered Value	imps79b	Total Frequency
1	1	1231
2	0	372

The GLIMMIX procedure is modeling the probability that imps79b='1'.

Dimensions

G-side Cov. Parameters	1
Columns in X	4
Columns in Z per Subject	1
Subjects (Blocks in V)	437
Max Obs per Subject	5

Optimization Information

Optimization Technique	Dual Quasi-Newton
Parameters in Optimization	5
Lower Boundaries	1
Upper Boundaries	0
Fixed Effects	Not Profiled
Starting From	GLM estimates
Quadrature Points	7

Iteration History

Iteration	Restarts	Evaluations	Objective Function	Change	Max Gradient
0	0	4	1301.9906335	.	60.97944
1	0	2	1263.9445041	38.04612941	25.65002
2	0	4	1263.3746592	0.56984495	30.57276
....					

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

Fit Statistics

-2 Log Likelihood	1249.69
AIC (smaller is better)	1259.69
AICC (smaller is better)	1259.73
BIC (smaller is better)	1280.09
CAIC (smaller is better)	1285.09
HQIC (smaller is better)	1267.74

Fit Statistics for Conditional Distribution

-2 log L(imps79b | r. effects)	674.27
Pearson Chi-Square	911.19
Pearson Chi-Square / DF	0.57

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
Intercept	id	4.4825	0.9450

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	5.3857	0.6299	435	8.55	<.0001
tx	-0.02140	0.6529	1164	-0.03	0.9739
sweek	-1.4973	0.2905	1164	-5.15	<.0001
tx*sweek	-1.0183	0.3342	1164	-3.05	0.0024

Type III Tests of Fixed Effects

Effect	Num DF	Den DF	F Value	Pr > F
tx	1	1164	0.00	0.9739
sweek	1	1164	26.56	<.0001
tx*sweek	1	1164	9.28	0.0024

```
                 Tests of Covariance Parameters
                    Based on the Likelihood

Label                          DF    -2 Log Like      ChiSq    Pr > ChiSq    Note

test of random intercept        1        1362.06     112.37        <.0001    MI

MI: P-value based on a mixture of chi-squares.
```

Comparing mixed logistic to ordinary (fixed) logistic regression
$H_0 : \sigma^2_{\upsilon_0} = 0, \quad H_A : \sigma^2_{\upsilon_0} > 0 \quad \Rightarrow$ one-sided test

mixture refers to a 50:50 mixture of a χ^2_0 and a χ^2_1 distribution; chi-bar square distribution; p-value is obtained from χ^2_1, but is halved

```
/* random trend logistic regression via GLIMMIX */
PROC GLIMMIX DATA=one METHOD=QUAD  NOCLPRINT;
CLASS id;
MODEL imps79b(DESC) = tx sweek tx*sweek / SOLUTION DIST=BINARY LINK=LOGIT;
RANDOM INTERCEPT sweek / SUBJECT=id TYPE=UN GCORR SOLUTION;
ODS OUTPUT SOLUTIONR=ebest2;
COVTEST 'test of random effects' GLM;
COVTEST 'test of random slope' . 0 0;

/* print out the estimated random effects */
PROC PRINT DATA=ebest2;
RUN;
```

- `COVTEST 'test of random effects' GLM;`
  will compare this model to model without random effects using LR test:
  $H_0 : \sigma^2_{\upsilon_0} = \sigma^2_{\upsilon_1} = \sigma_{\upsilon_{01}} = 0$
- `COVTEST 'test of random slope' .  0 0;`
  will compare this model to model without random slope and intercept slope covariance using LR test: $H_0 : \sigma^2_{\upsilon_1} = \sigma_{\upsilon_{01}} = 0$
- `SOLUTION` on `RANDOM` statement will list the estimates of the random effects

Fit Statistics

-2 Log Likelihood	1227.41
AIC (smaller is better)	1241.41
AICC (smaller is better)	1241.48
BIC (smaller is better)	1269.97
CAIC (smaller is better)	1276.97
HQIC (smaller is better)	1252.68

Estimated G Correlation Matrix

Effect	Row	Col1	Col2
Intercept	1	1.0000	-0.4527
sweek	2	-0.4527	1.0000

Covariance Parameter Estimates

Cov Parm	Subject	Estimate	Standard Error
UN(1,1)	id	6.9816	2.9281
UN(2,1)	id	-2.1027	1.2241
UN(2,2)	id	3.0906	1.1842

Solutions for Fixed Effects

Effect	Estimate	Standard Error	DF	t Value	Pr > |t|
Intercept	5.9323	0.9481	435	6.26	<.0001
tx	0.2882	0.7436	727	0.39	0.6985
sweek	-1.4042	0.4734	437	-2.97	0.0032
tx*sweek	-1.6115	0.4806	727	-3.35	0.0008

Solution for Random Effects

Effect	Subject	Estimate	Std Err Pred	DF	t Value	Pr > |t|
Intercept	id 1103	-3.5747	2.1974	727	-1.63	0.1042
sweek	id 1103	1.5078	1.2532	727	1.20	0.2293
Intercept	id 1104	-2.4664	2.1680	727	-1.14	0.2556
sweek	id 1104	-0.7525	1.6193	727	-0.46	0.6423
Intercept	id 1105	-2.4732	2.1699	727	-1.14	0.2548
sweek	id 1105	-0.7363	1.6370	727	-0.45	0.6530

Tests of Covariance Parameters
Based on the Likelihood

Label	DF	-2 Log Like	ChiSq	Pr > ChiSq	Note
test of random effects	3	1362.06	134.66	<.0001	--
test of random slope	2	1249.73	22.33	<.0001	MI

MI: P-value based on a mixture of chi-squares.
--: Standard test with unadjusted p-values.

- `test of random effects` compares random trend model to ordinary logistic regression using ordinary LR test (too conservative)

- `test of random slope` compares random trend to random intercept model

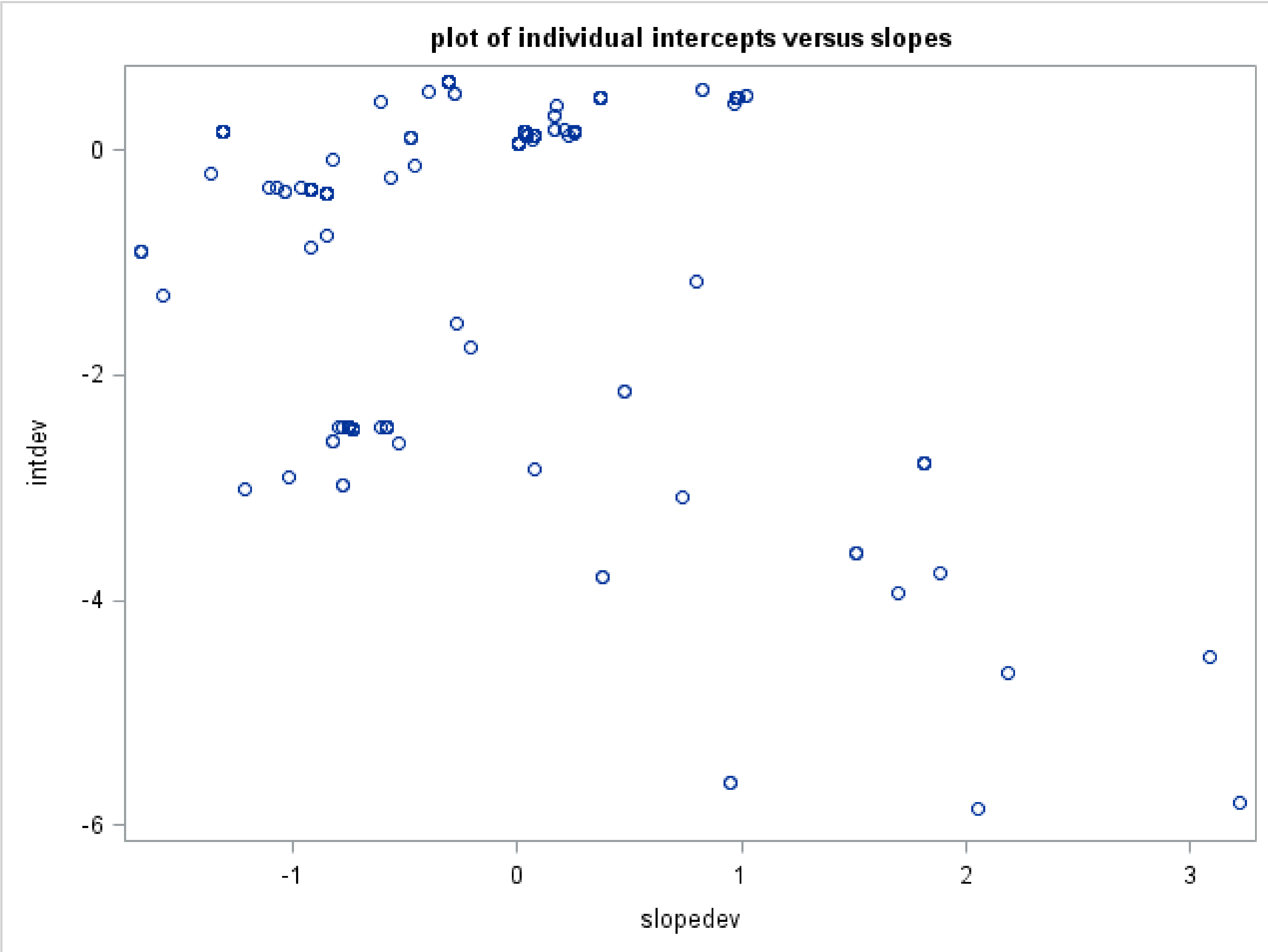
  $H_0 : \sigma^2_{\upsilon_1} = \sigma_{\upsilon_{01}} = 0$

  uses `chibar2(12)`, 50:50 mixture of a χ^2_1 and a χ^2_2 distribution; p-value is obtained from the average of χ^2_1 and χ^2_2 (i.e., q and $q-1$, where q is the number of (co)variance parameters in the null)

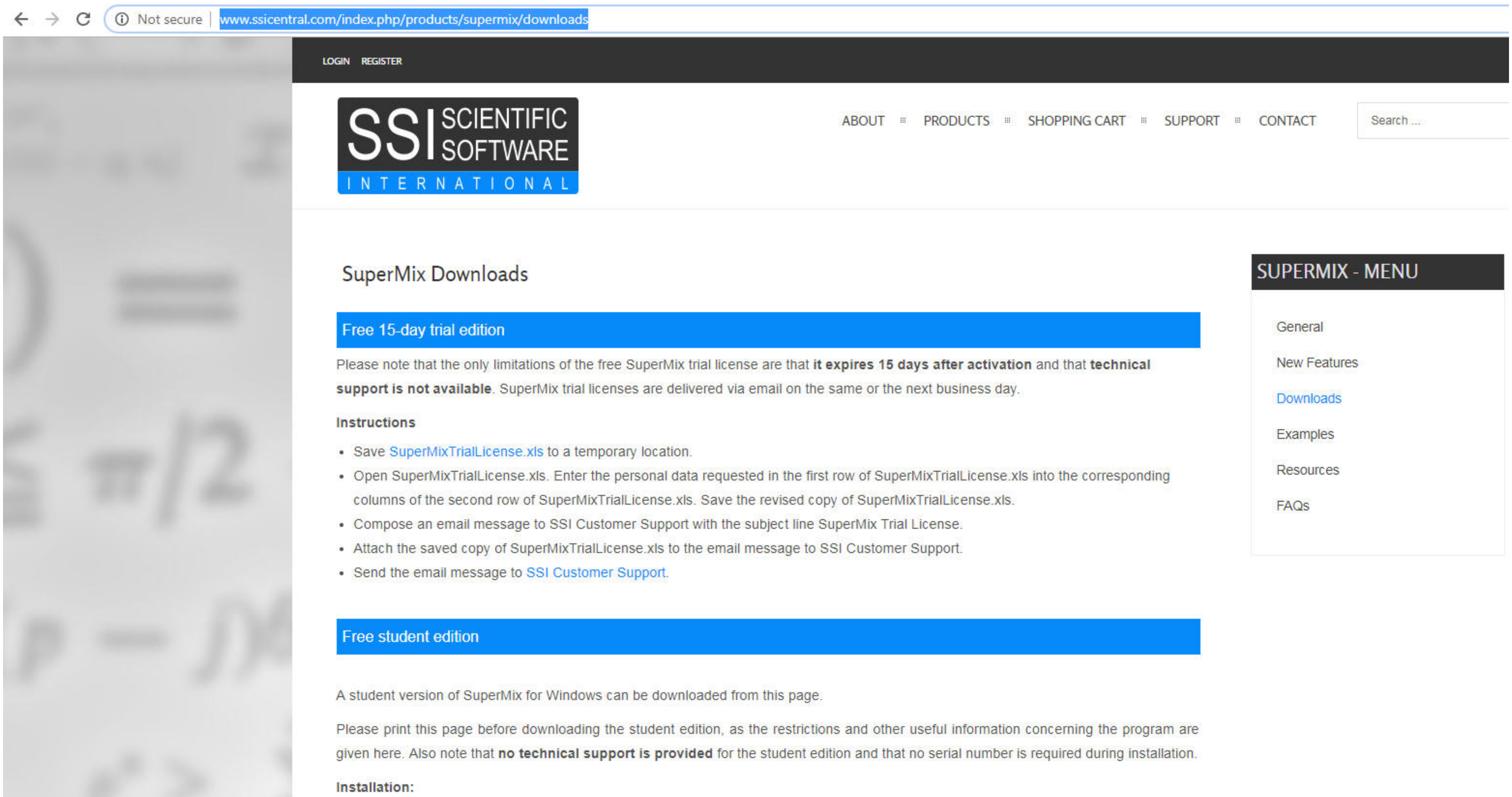
```
/* print out the estimated random effects */
PROC PRINT DATA=ebest2;
RUN;
```

Obs	Effect	Subject	Estimate	StdErr Pred	DF	tValue	Probt
1	Intercept	id 1103	-3.5747	2.1974	727	-1.63	0.1042
2	sweek	id 1103	1.5078	1.2532	727	1.20	0.2293
3	Intercept	id 1104	-2.4664	2.1680	727	-1.14	0.2556
4	sweek	id 1104	-0.7525	1.6193	727	-0.46	0.6423
5	Intercept	id 1105	-2.4732	2.1699	727	-1.14	0.2548
6	sweek	id 1105	-0.7363	1.6370	727	-0.45	0.6530
7	Intercept	id 1106	-5.6168	1.9482	727	-2.88	0.0041
8	sweek	id 1106	0.9518	1.4954	727	0.64	0.5247

```
DATA randest2 (KEEP=subject intdev slopedev);
     ARRAY y(2) intdev slopedev;
     DO par = 1 TO 2;
        SET ebest2;
        BY subject;
        y(par) = ESTIMATE;
        IF LAST.id THEN RETURN;
     END;

PROC SGPLOT  DATA=randest2;
     SCATTER X=slopedev Y=intdev;
     TITLE2 'plot of individual intercepts versus slopes';
RUN;
```

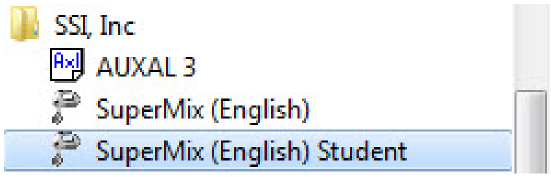


plot of individual intercepts versus slopes
intdev
0
-2
-4
-6
-1
0
1
2
3
slopedev

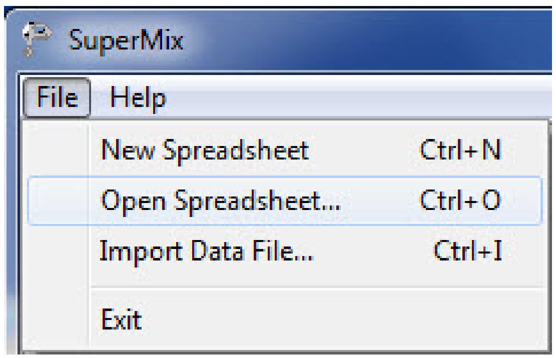


Free student version of Supermix (for Windows) at www.ssicentral.com/index.php/products/supermix/downloads

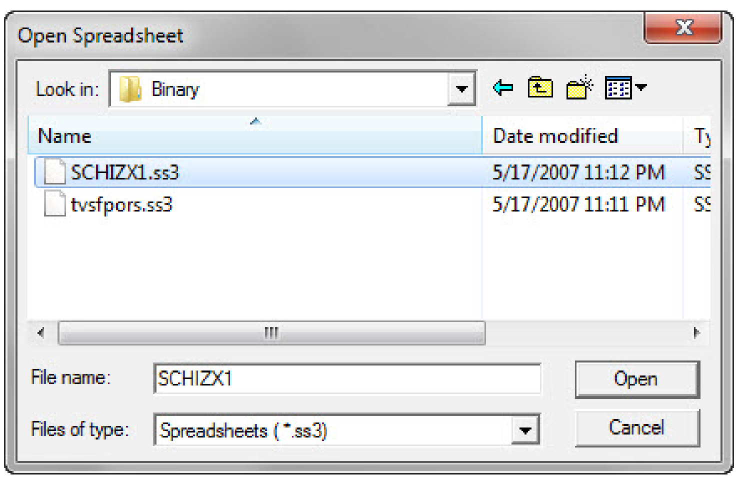
- Under SSI, Inc > “SuperMix (English)” or “SuperMix (English) Student”



- 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

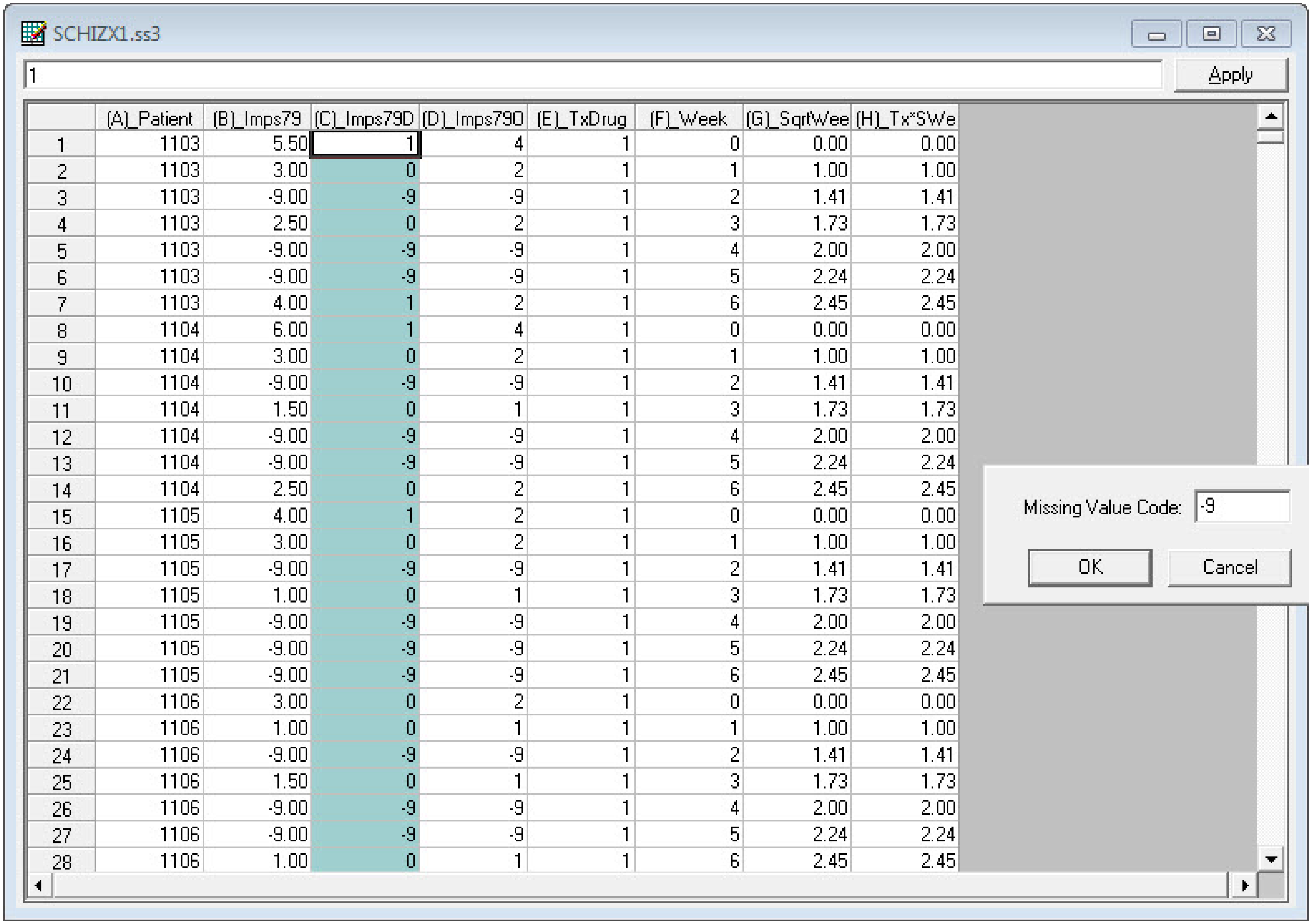
SCHIZX1.ss3

1103

Apply

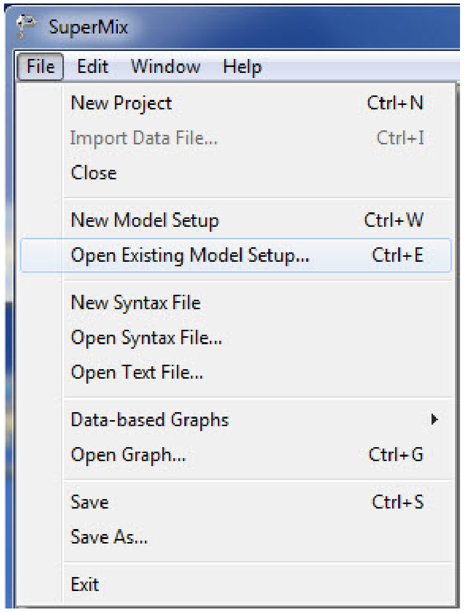
	(A)_Patient	(B)_Imps79	(C)_Imps79D	(D)_Imps790	(E)_TxDrug	(F)_Week	(G)_SqrtWee	(H)_Tx*SWe
1	1103	5.50	1	4	1	0	0.00	0.00
2	1103	3.00	0	2	1	1	1.00	1.00
3	1103	-9.00	-9	-9	1	2	1.41	1.41
4	1103	2.50	0	2	1	3	1.73	1.73
5	1103	-9.00	-9	-9	1	4	2.00	2.00
6	1103	-9.00	-9	-9	1	5	2.24	2.24
7	1103	4.00	1	2	1	6	2.45	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"



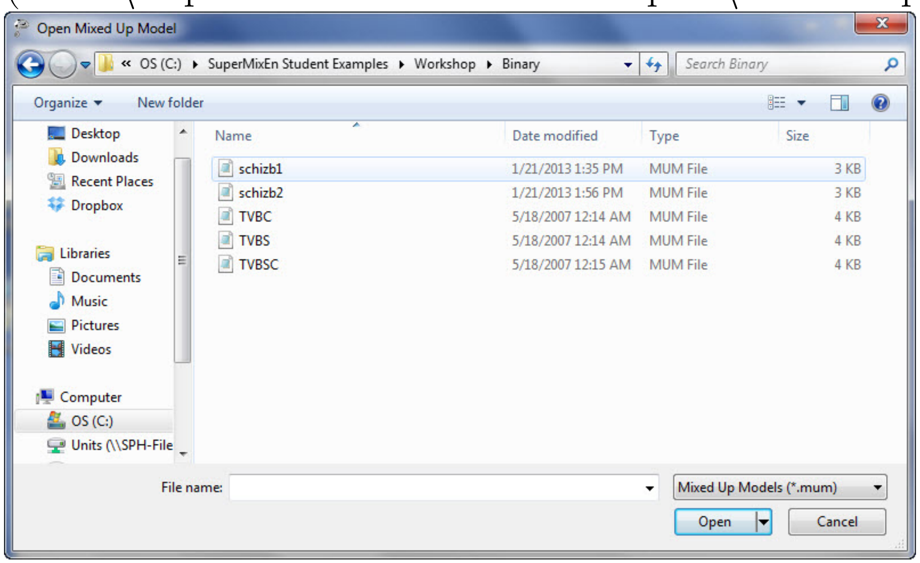
	(A)_Patient	(B)_Imps79	(C)_Imps79D	(D)_Imps79O	(E)_TxDrug	(F)_Week	(G)_SqrtWee	(H)_Tx*SWe
1	1103	5.50	1	4	1	0	0.00	0.00
2	1103	3.00	0	2	1	1	1.00	1.00
3	1103	-9.00	-9	-9	1	2	1.41	1.41
4	1103	2.50	0	2	1	3	1.73	1.73
5	1103	-9.00	-9	-9	1	4	2.00	2.00
6	1103	-9.00	-9	-9	1	5	2.24	2.24
7	1103	4.00	1	2	1	6	2.45	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

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

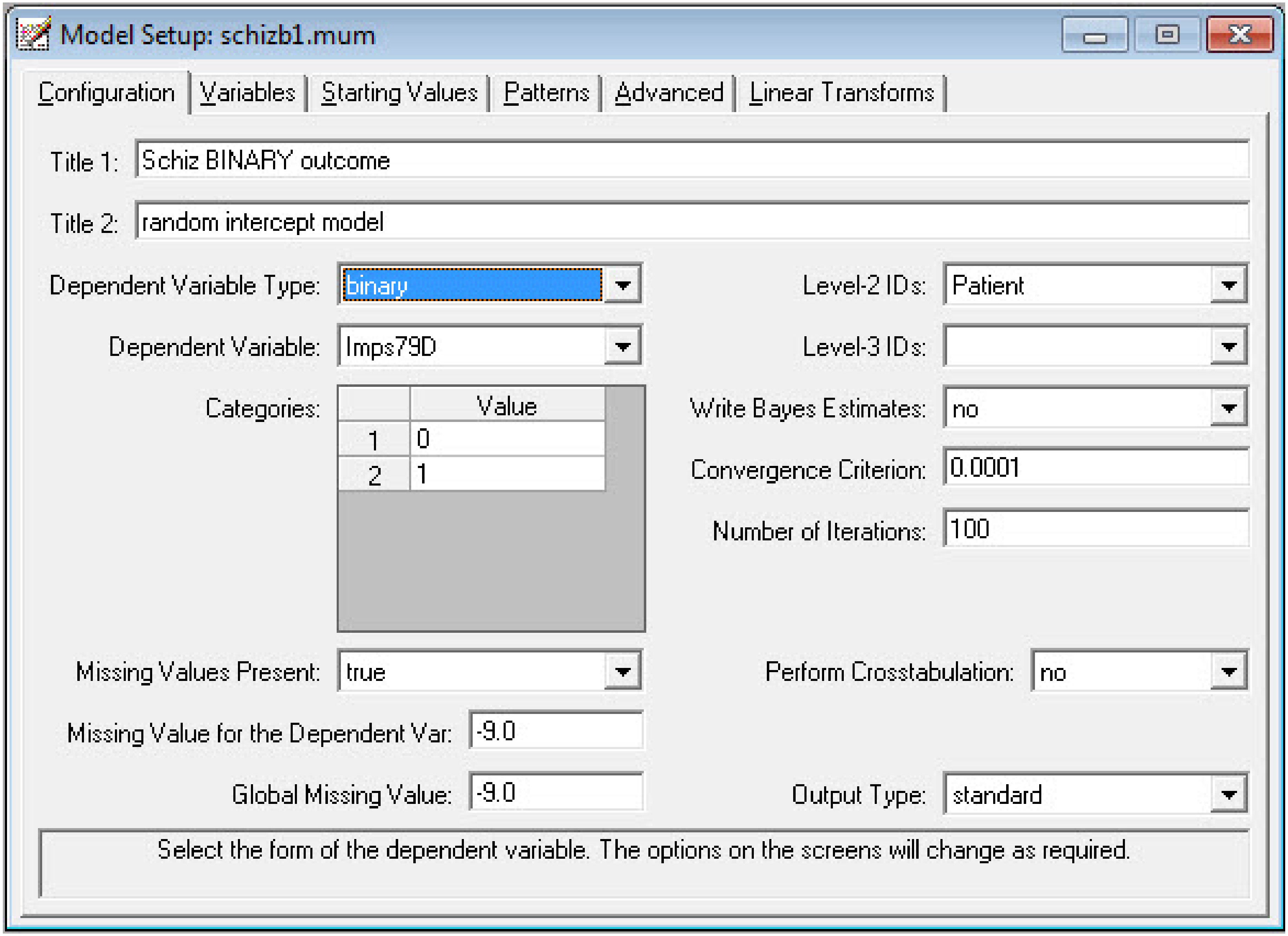


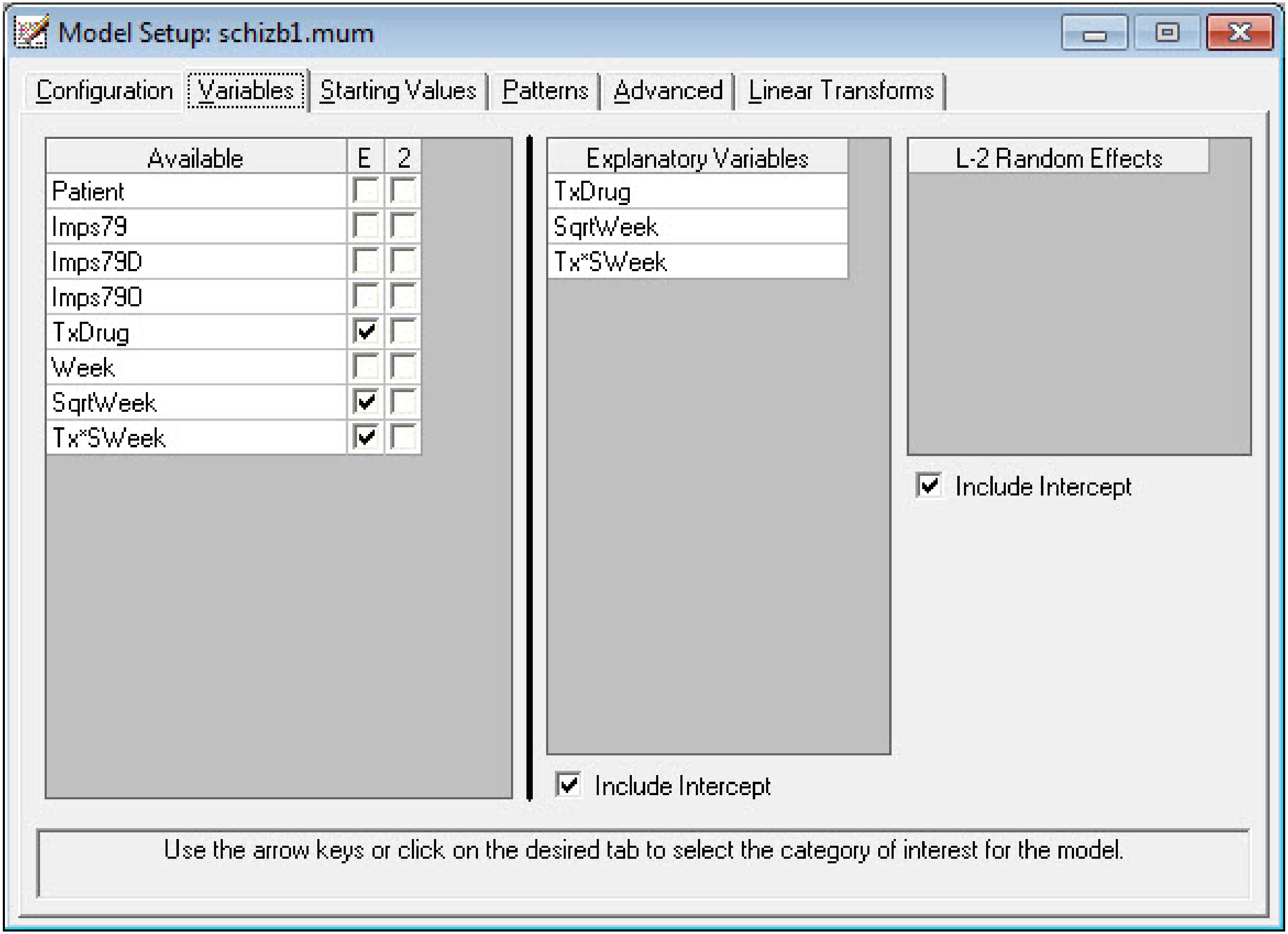
Open C:\SuperMixEn Examples\Workshop\Binary\schizb1.mum

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

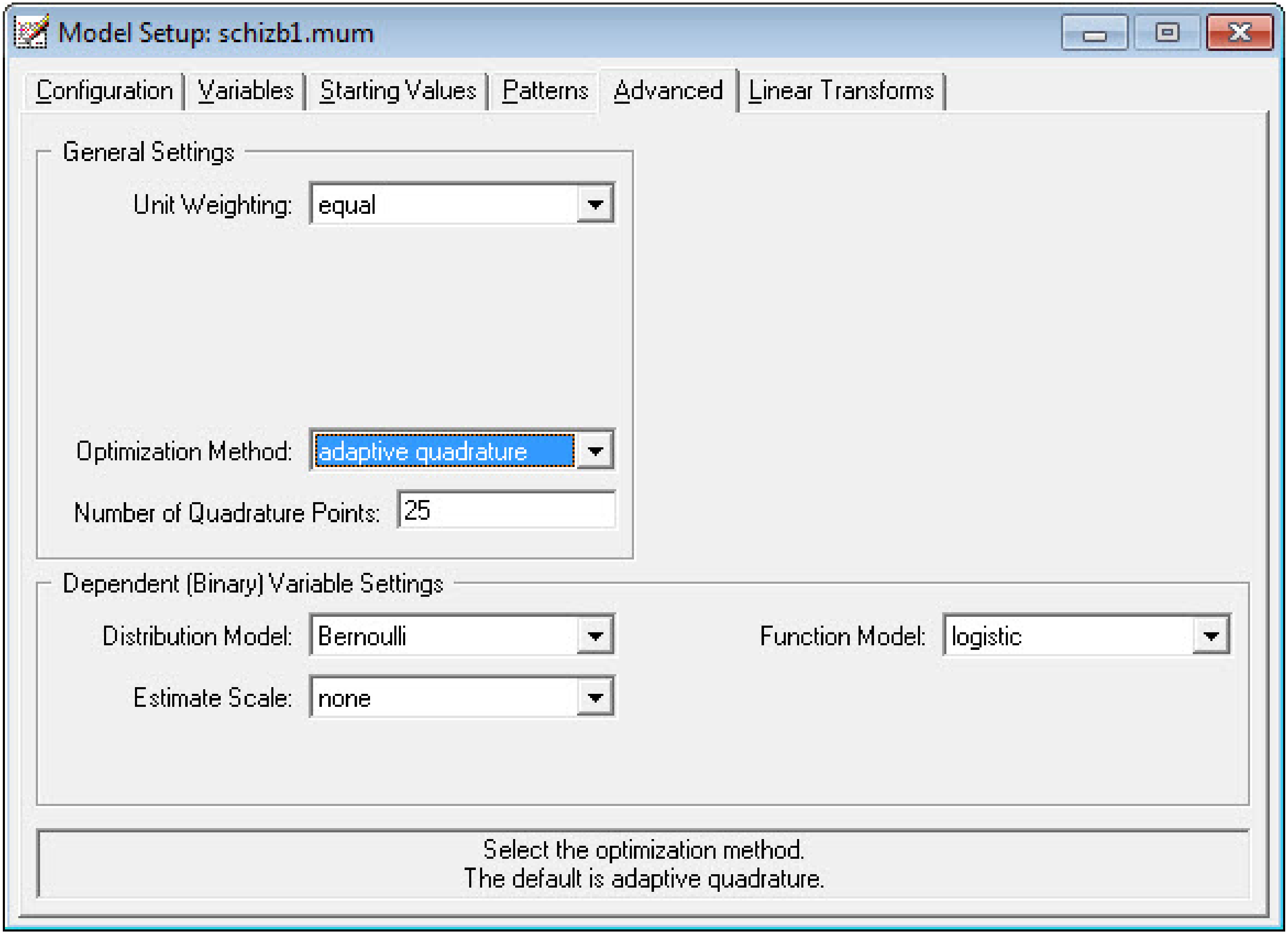


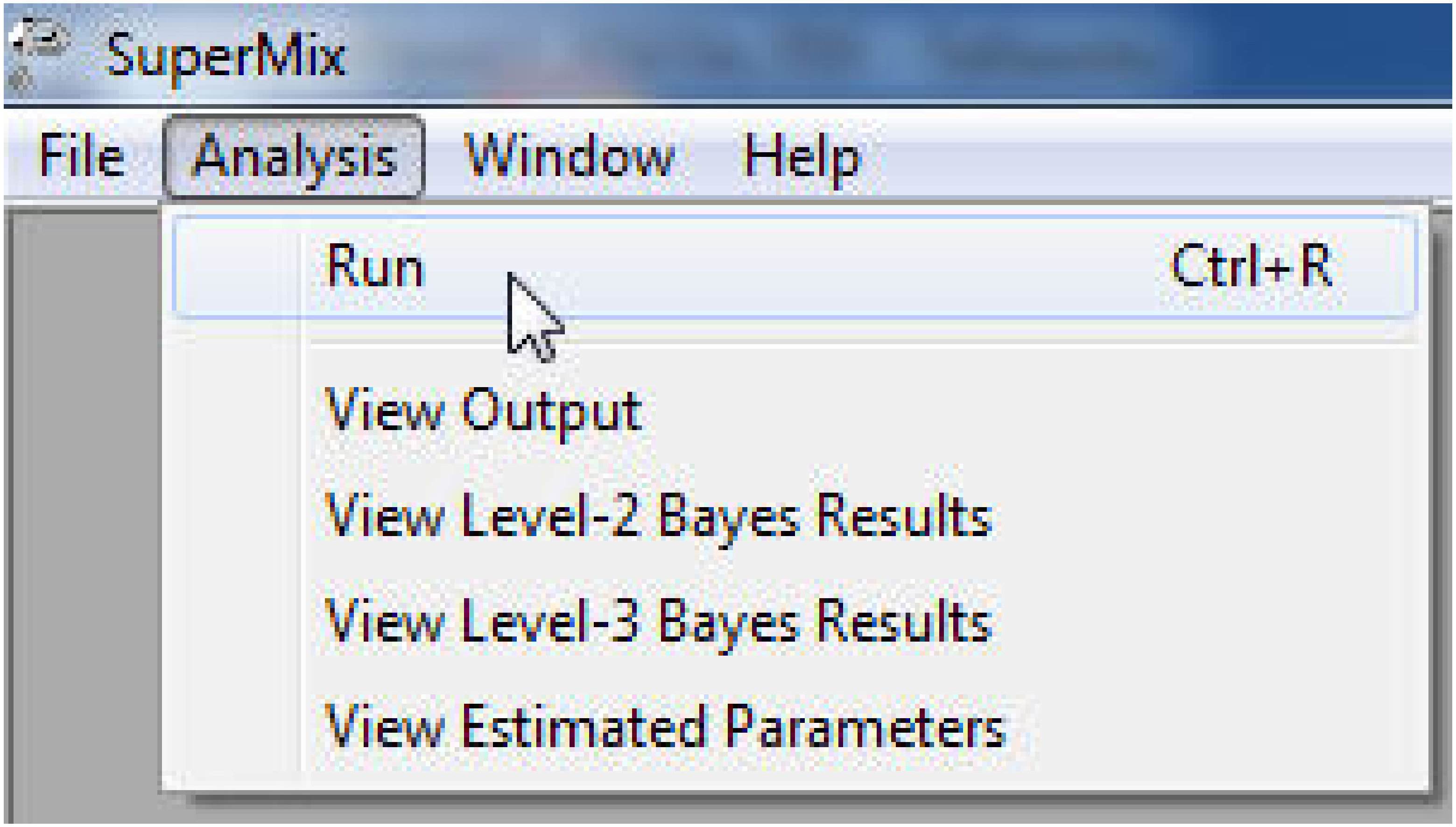
Note “Dependent Variable Type” should be “binary”




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
Include Intercept
L-2 Random Effects
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"




SuperMix
File
Analysis
Window
Help
Run
Ctrl+R
View Output
View Level-2 Bayes Results
View Level-3 Bayes Results
View Estimated Parameters

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

			Bounds	
Parameter	Estimate	Odds Ratio	Lower	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

Save As... Close

schizb1.out

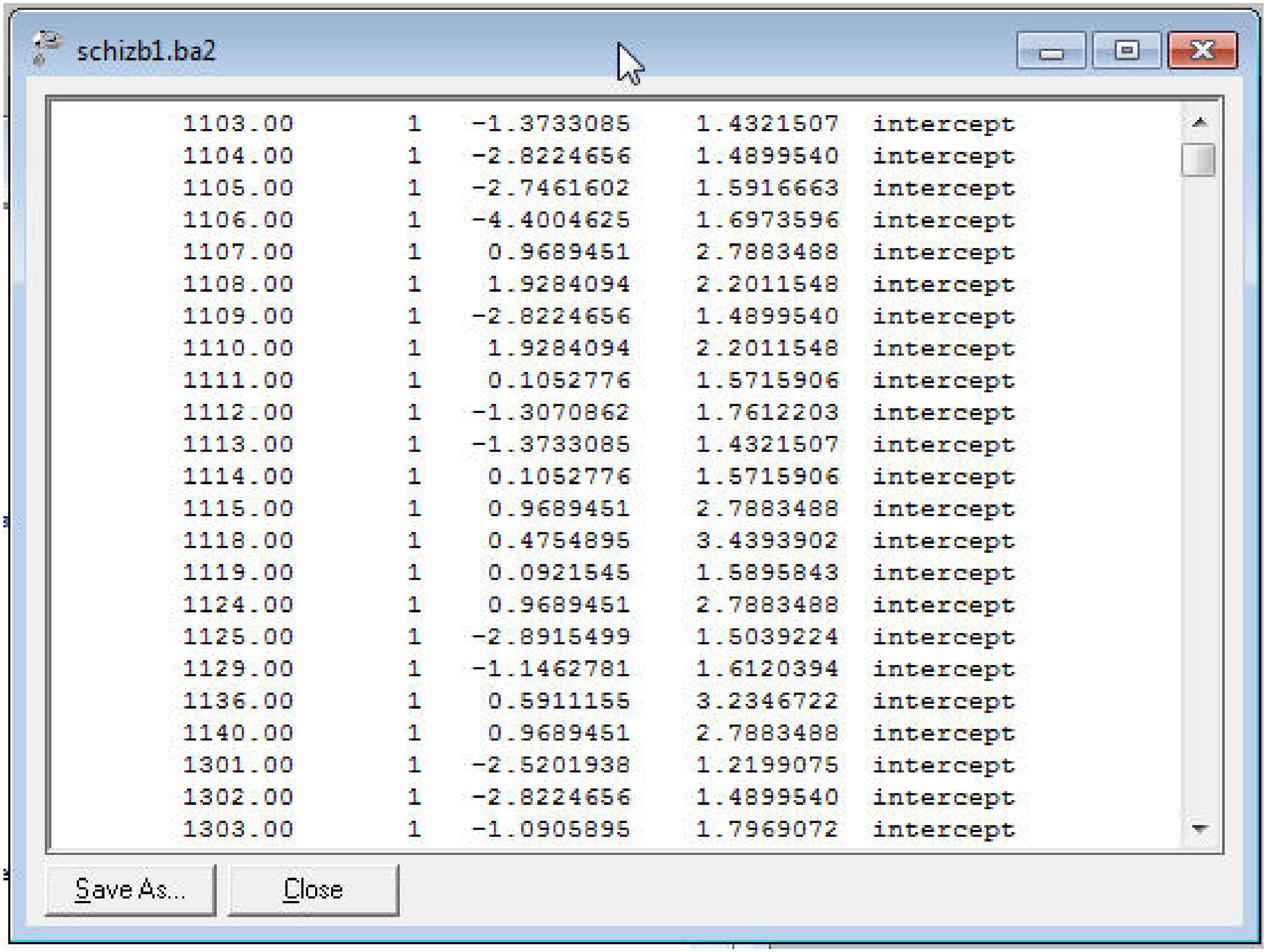
```
Calculation of the intracluster correlation
-------------------------------------------
residual variance = pi*pi / 3 (assumed)
cluster  variance =     4.4781

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 up to 3-level models

Empirical Bayes Estimates of Random Effects

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

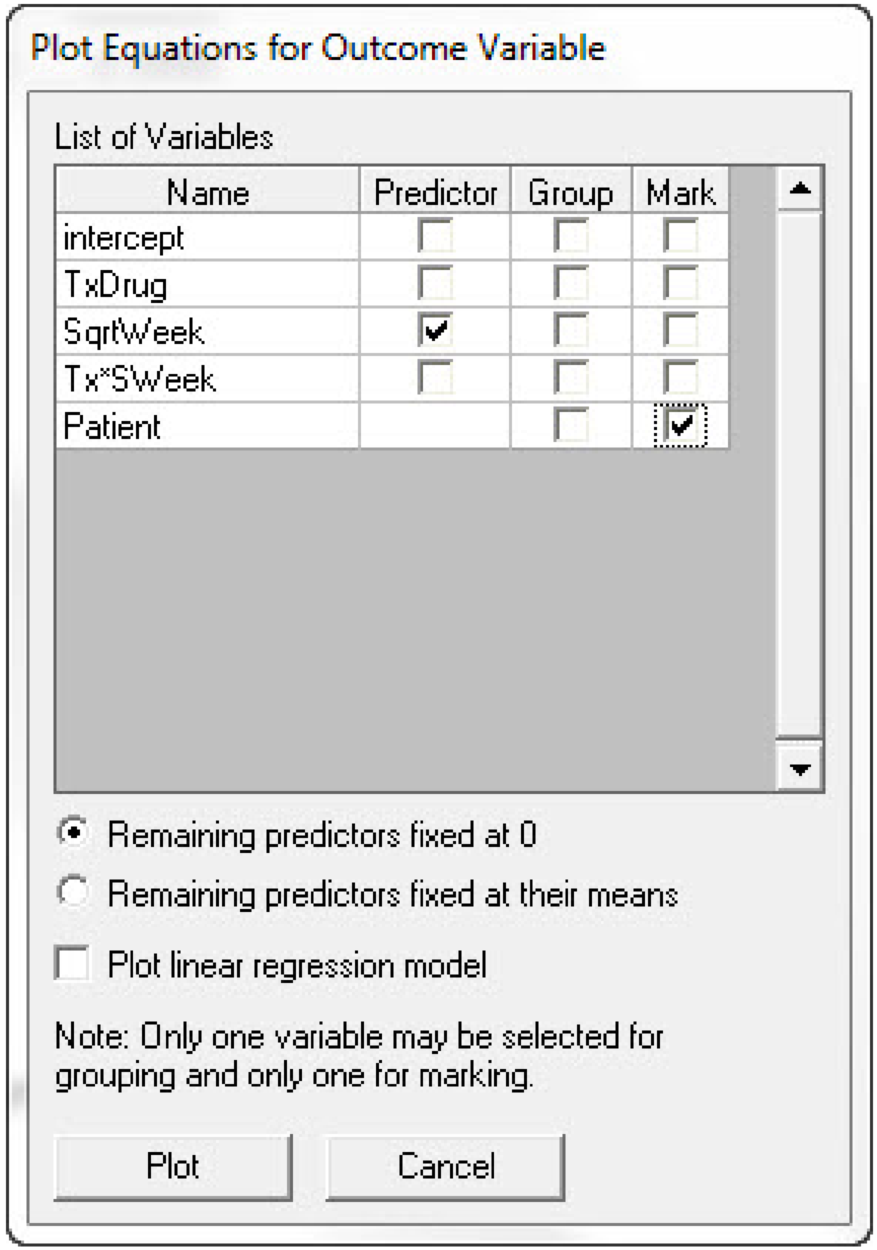

schizb1.ba2

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

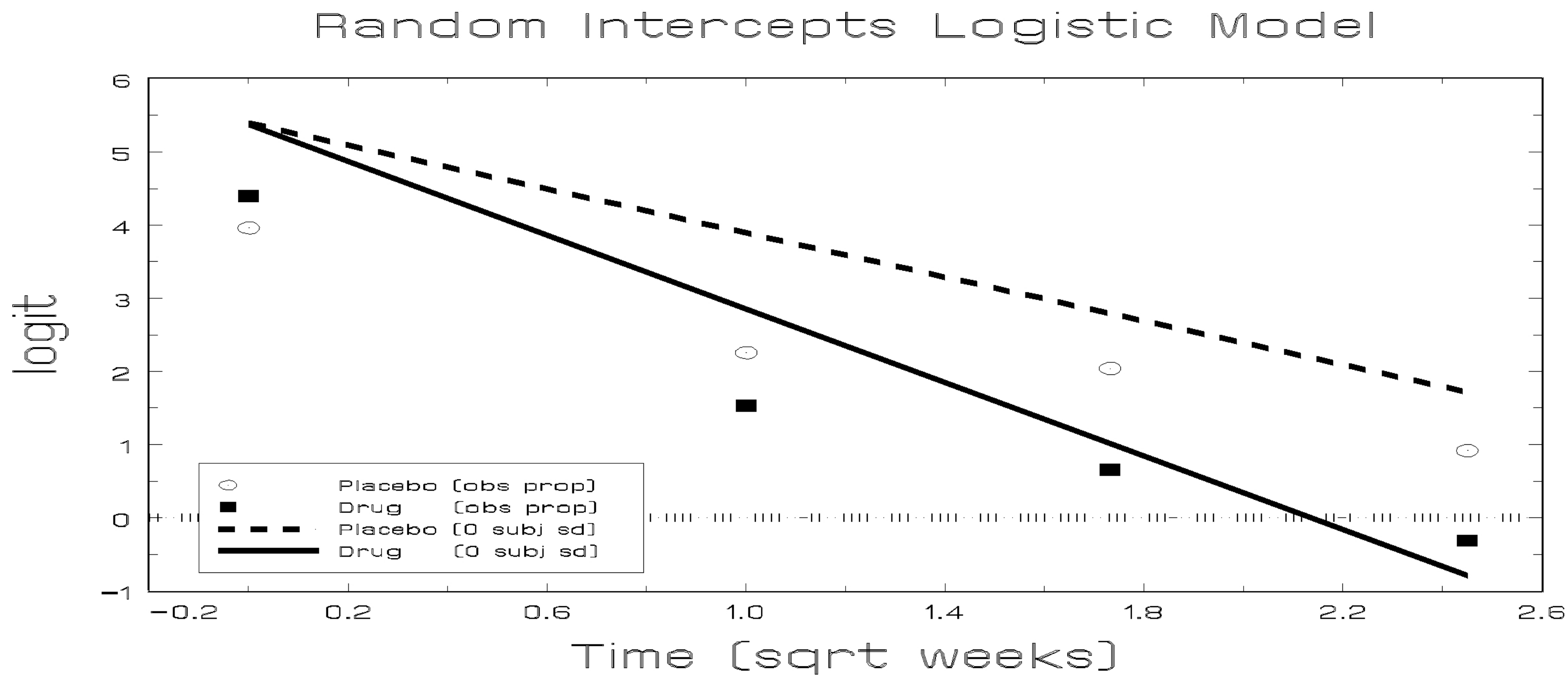
Save As... Close

ID, random effect number, estimate, variance, name

Select “Model-based Graphs” > “Equations”



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



$$
\begin{aligned}
\log\left[\frac{Pr(Y_{ij}=1)}{1-Pr(Y_{ij}=1)}\right] &= 5.39 - .03\,D_i - 1.50\,T_j - 1.01\,(D_i \times T_j) + \upsilon_{0i} \\
&\ \upsilon_{0i} \sim \mathcal{NID}(0, \hat{\sigma}_\upsilon^2 = 4.48)
\end{aligned}
$$

$\hat{\boldsymbol{\beta}}$ 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

β_0 = log odds of response for a typical subject with $\boldsymbol{x} = 0$ and $v_{0i} = 0$

$\boldsymbol{\beta}$ = log odds ratio for response associated with unit changes in $\boldsymbol{x}$ for the same subject value v_{0i}

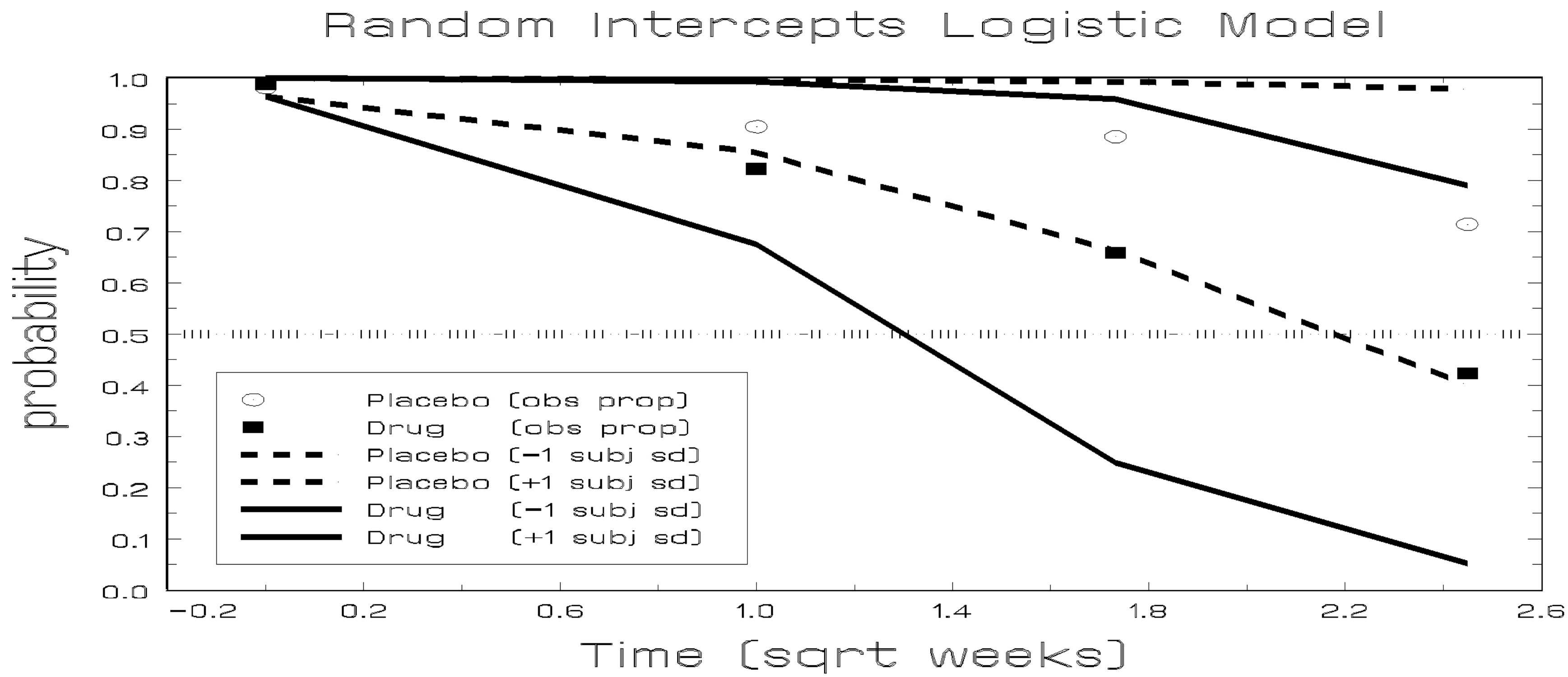
$*$ referred to as "subject-specific"

$*$ how a *subject's* response probability depends on $\boldsymbol{x}$

σ_v^2 = degree of heterogeneity across subjects in the probability of response not attributable to $\boldsymbol{x}$

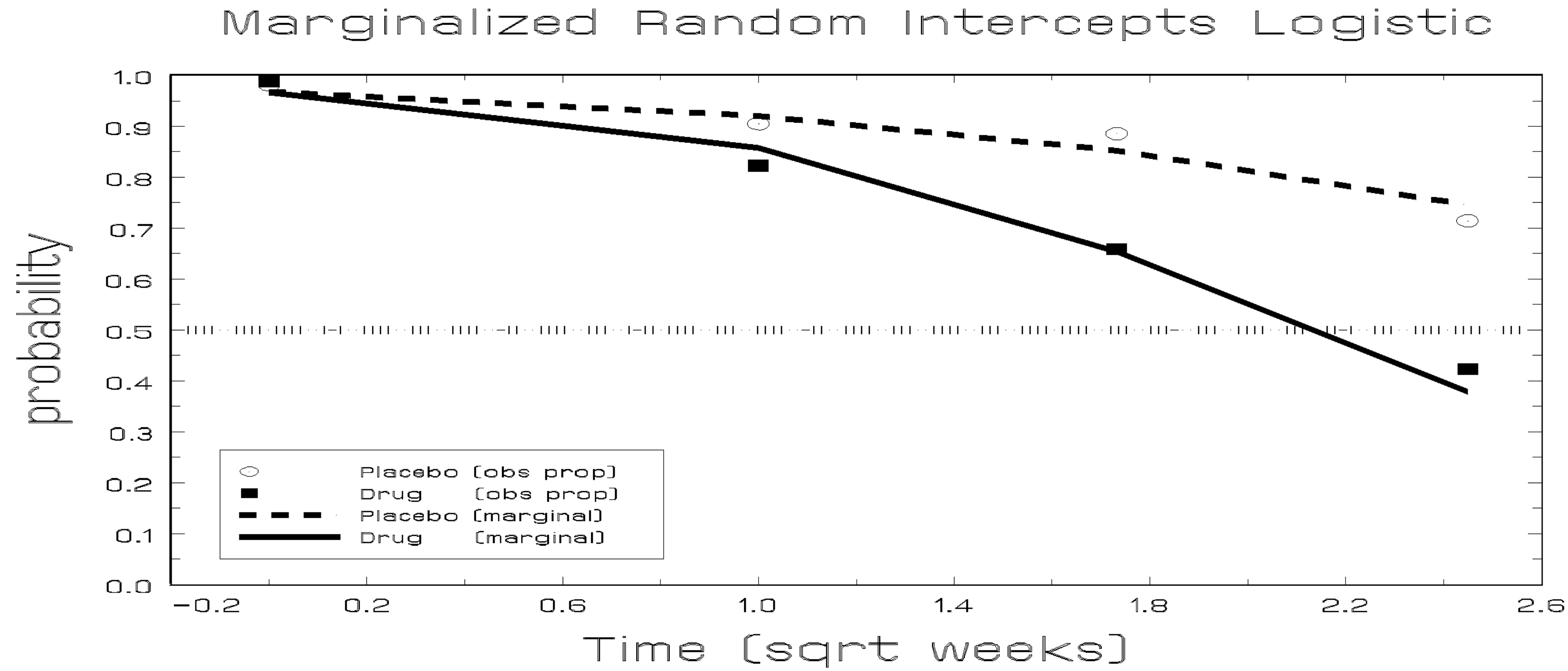
- most useful when the objective is to make inference about *subjects* rather than the population average
- interest is in the heterogeneity of subjects

Estimated Subject-Specific Probabilites



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

$$\text{where } \upsilon_{0i} = \begin{cases} -1\sigma_\upsilon \\ \ \ 1\sigma_\upsilon \end{cases} \text{ and } \hat{\sigma}_\upsilon = 2.12$$

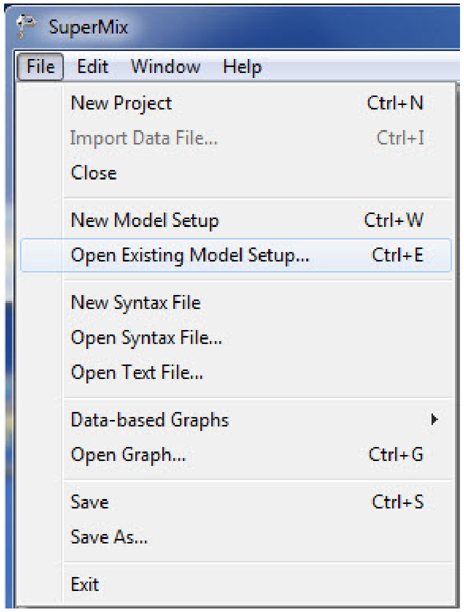


$$P(Y_{ij} = 1) = \frac{1}{1 + \exp\left[-\left(3.54 - .055\, D_i - 1.05\, T_j - .60\, D_i T_j\right)\right]}$$

$\Rightarrow$ obtained using the Population Average estimates from Supermix

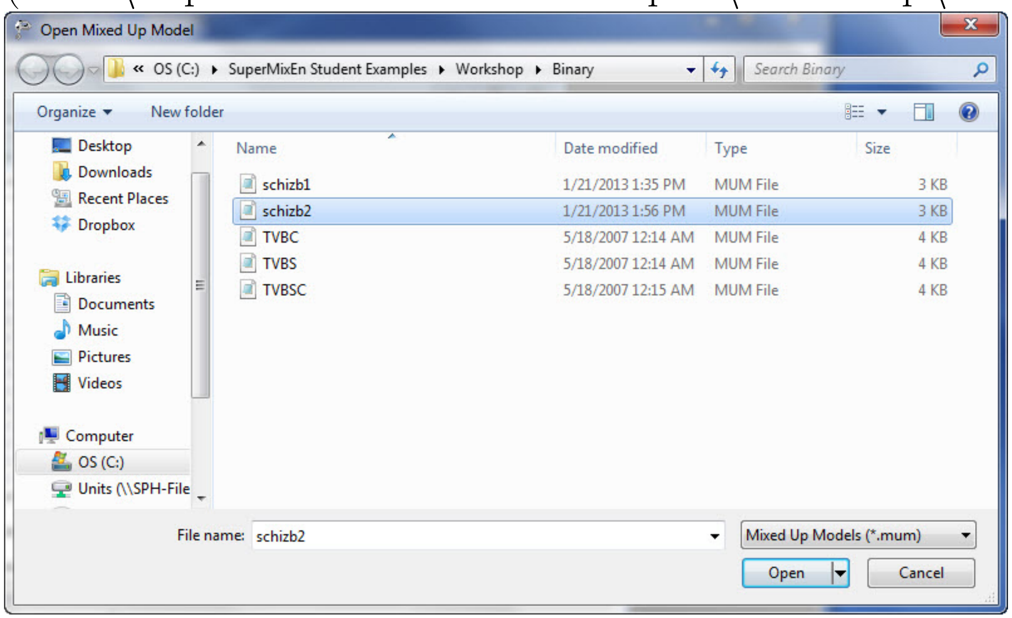
Hedeker D, du Toit SHC, Demirtas H, & Gibbons RD (2018). A note on marginalization of regression parameters from mixed models of binary outcomes. *Biometrics, 74(1)*:354-361.

Under “File” click on “Open Existing Model Setup”

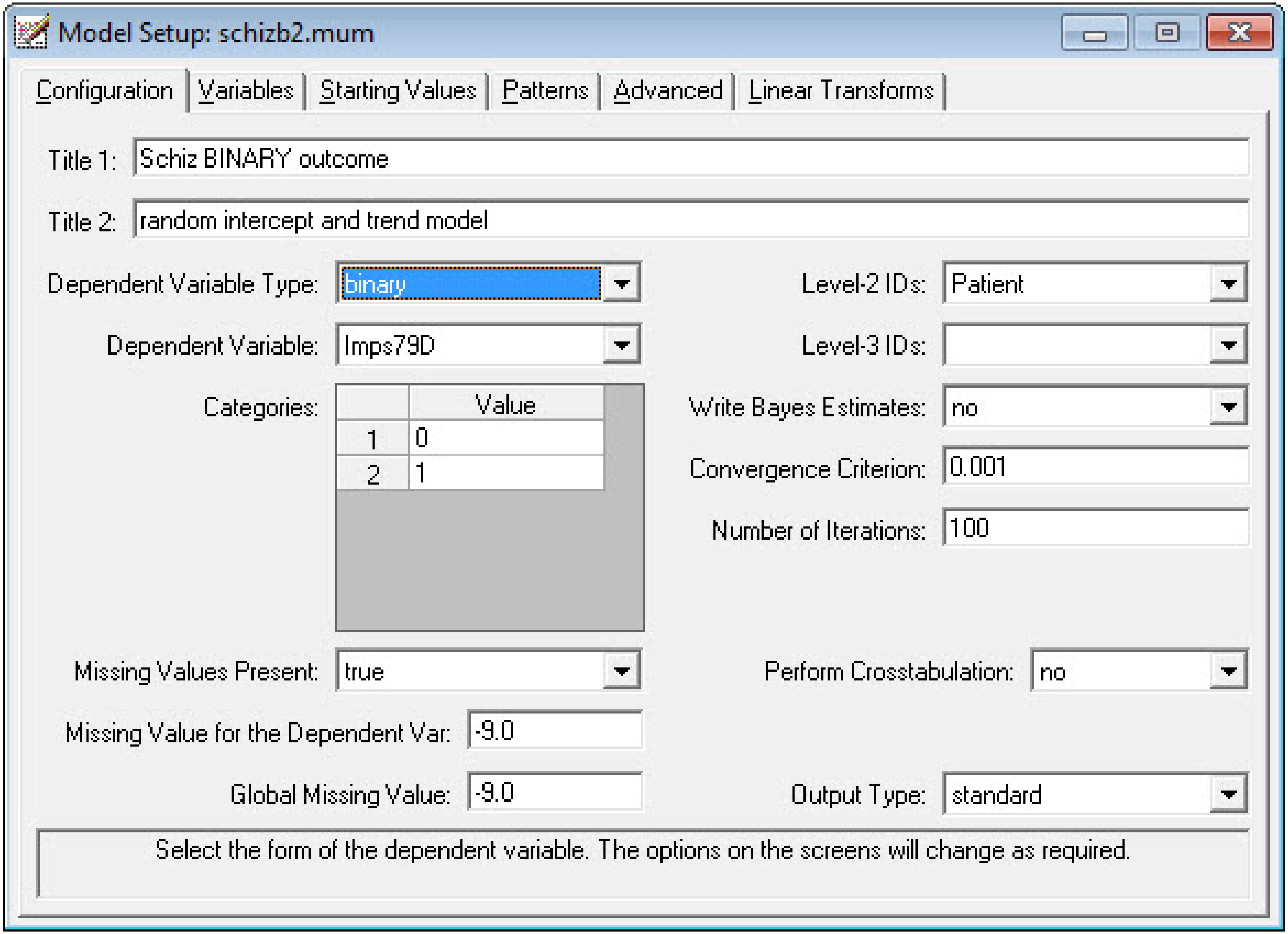


Open C:\SuperMixEn Examples\Workshop\Binary\schizb2.mum

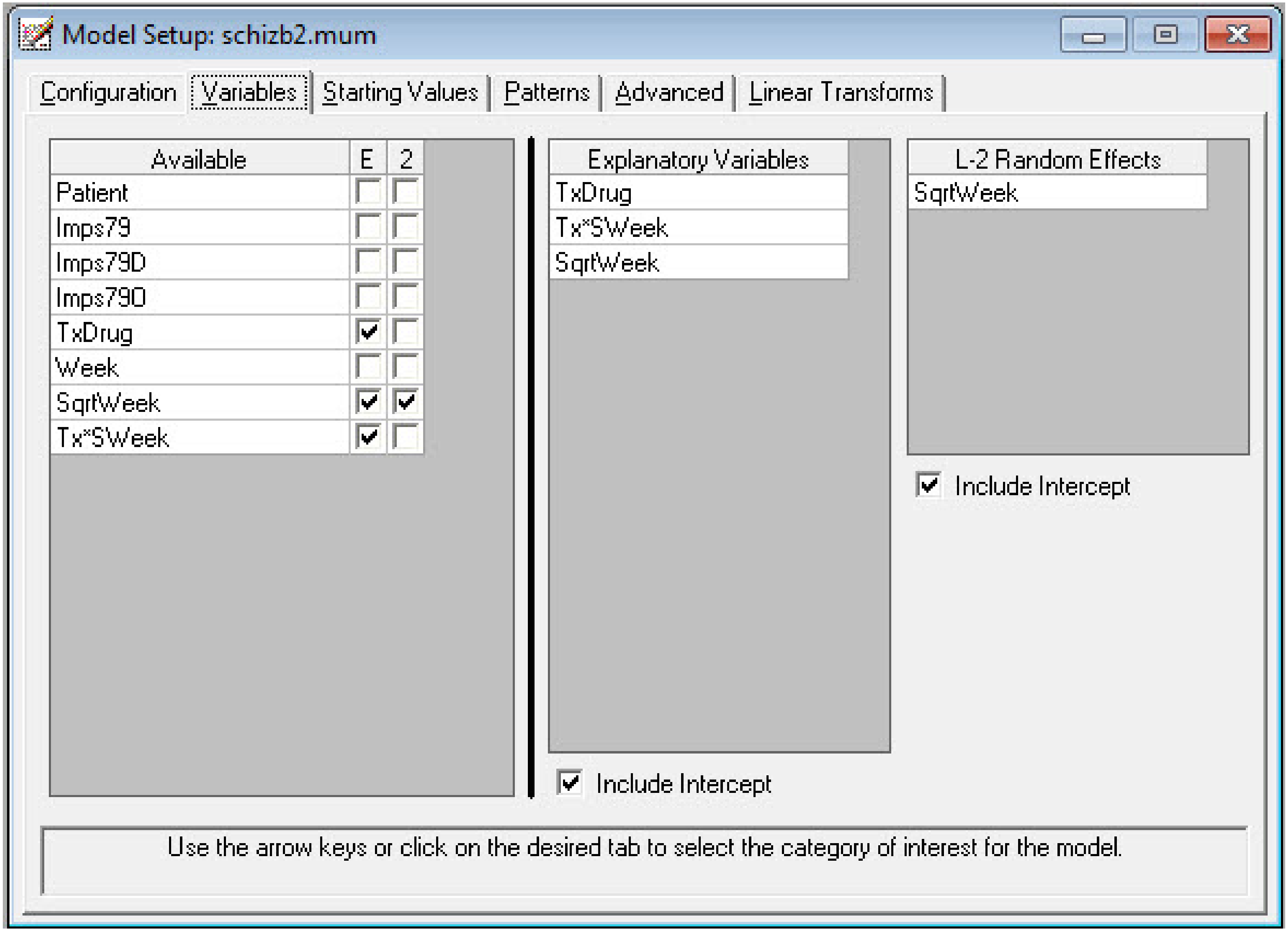
(or C:\SuperMixEn Student Examples\Workshop\Binary\schizb2.mum)



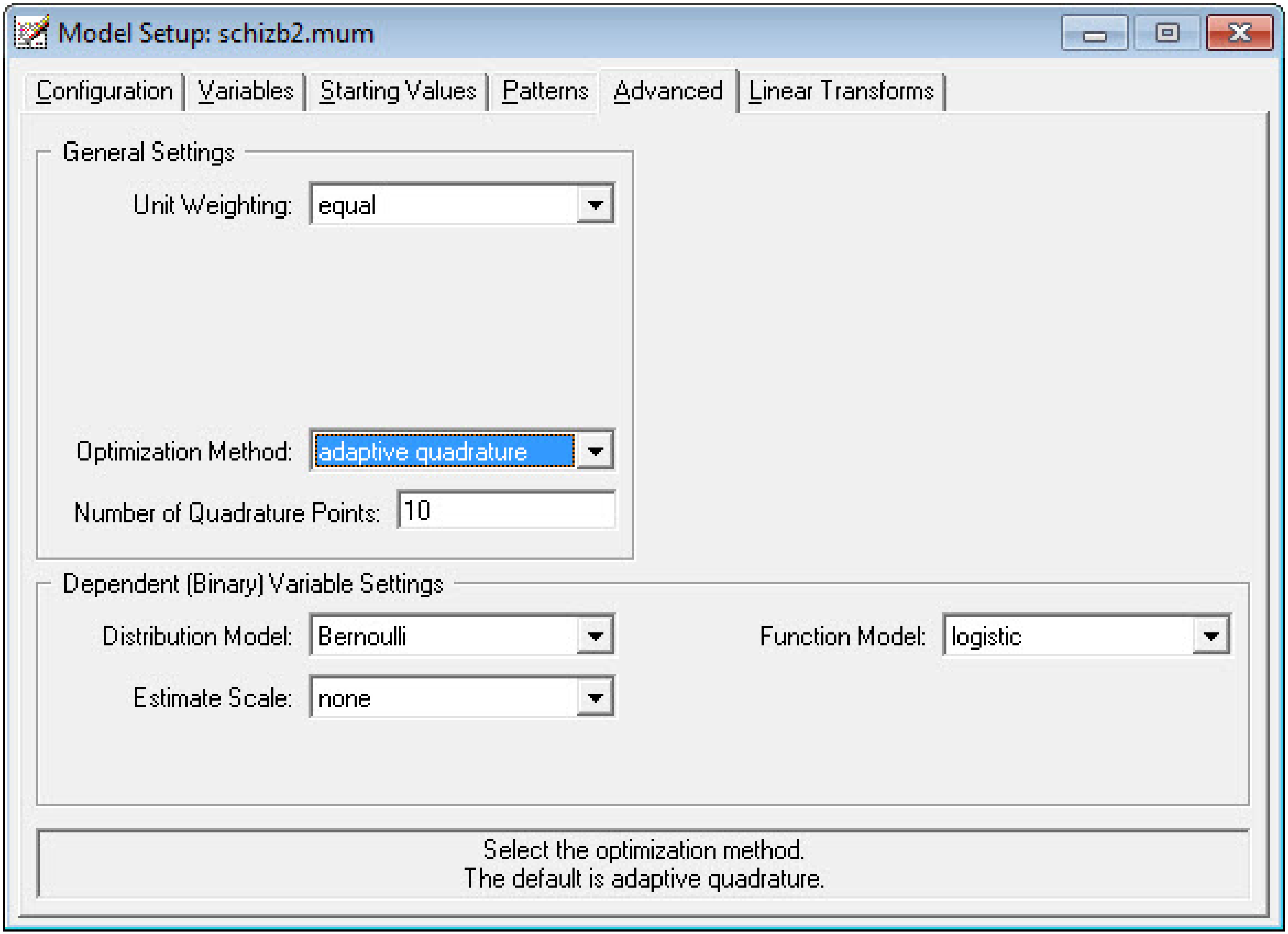
Note "Dependent Variable Type" should be "binary"



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

                                             Standard
Parameter               Estimate             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

                                                              Bounds
Parameter               Estimate           Odds Ratio       Lower        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

                                                  Standard
Parameter                        Estimate         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

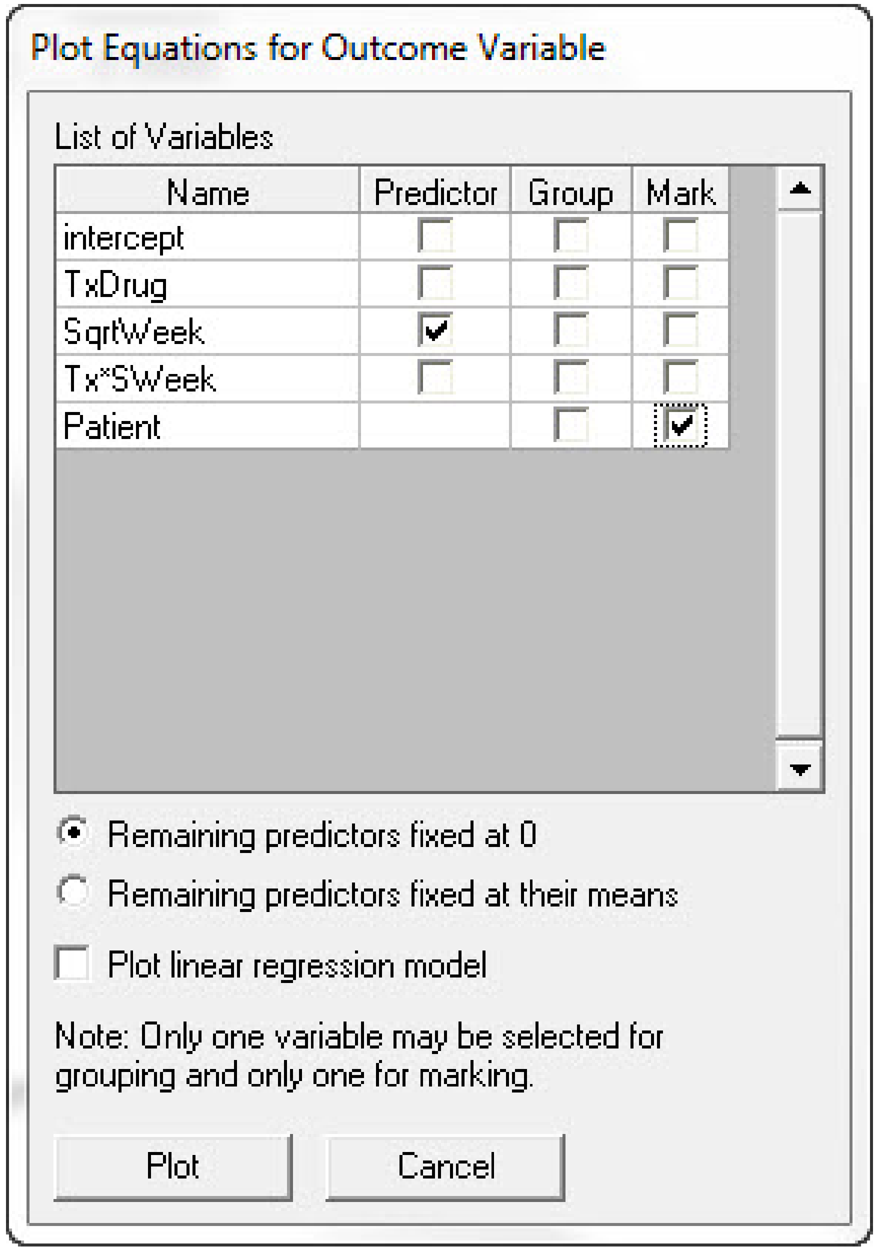
$\Rightarrow$ Comparing models: $H0: \sigma^2_{\upsilon_1} = \sigma_{\upsilon_{01}} = 0; \quad \chi^2_2 = 1249.73 - 1227.76 = 21.97, p < .001$

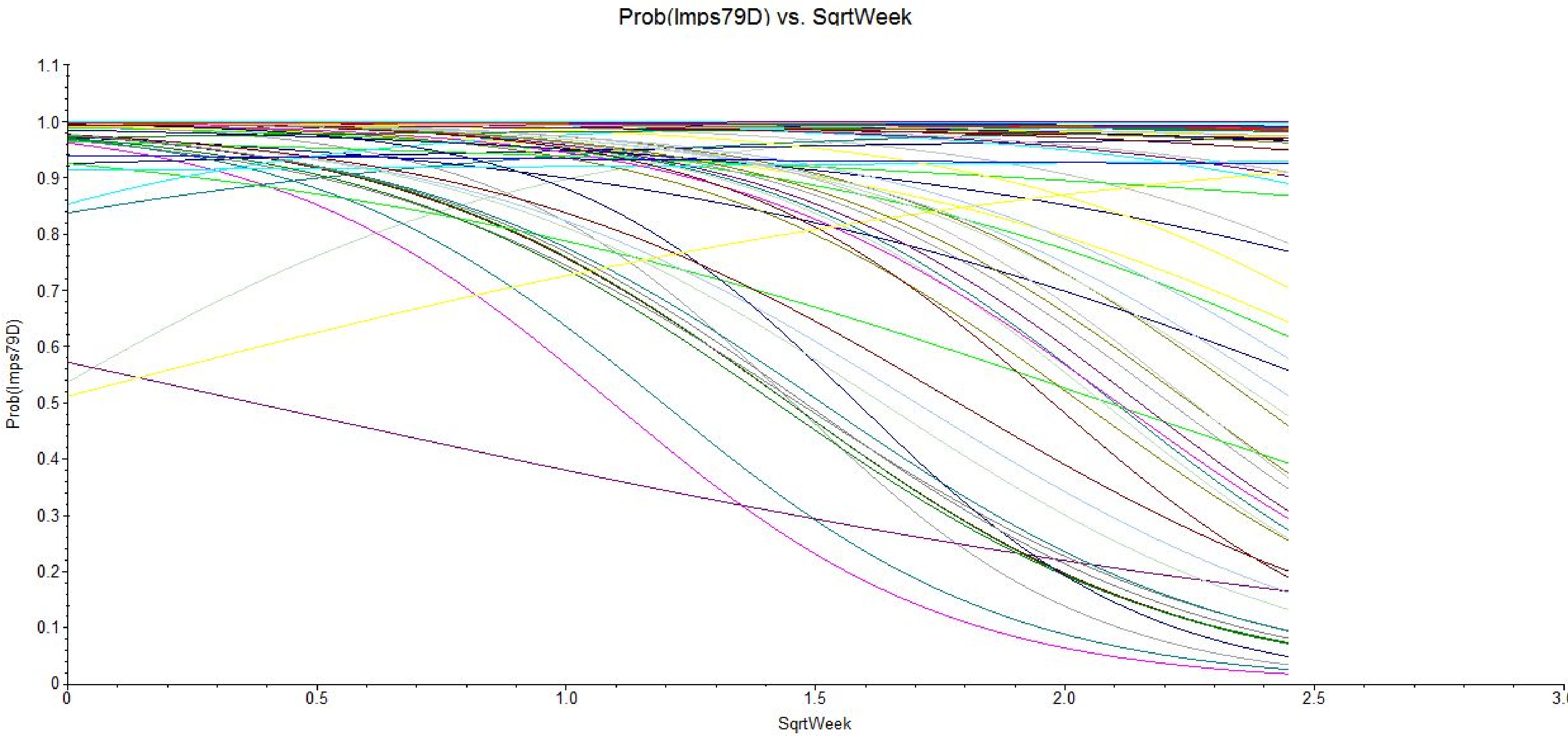
schizb2.out

```
                 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

Select “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
0.5
1.0
1.5
2.0
2.5
3.0

Supermix - 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
- yields both subject-specific (conditional) and population-average (marginal) estimates and inference of regression coefficients
- discrete/grouped time survival analysis via person-period dataset
  www.ssicentral.com/images/pdfs/Survival_clust.pdf