MLM 2007
Marginal vs RE models, Ordinal Responses (and other musings…)

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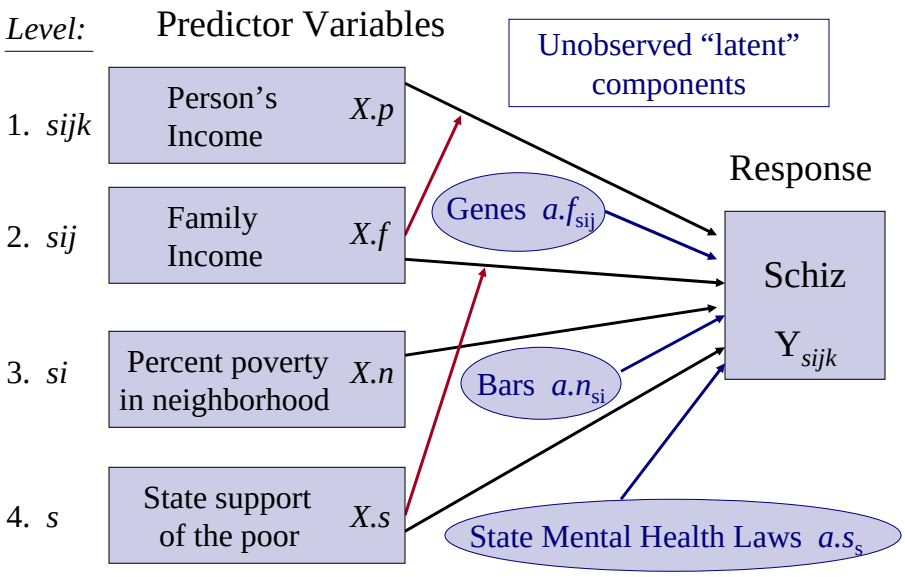
Guest Lecture

Discussion Outline

- MLM review: Goals & Concepts
- Marginal & Random-Effect Models:
  - Logistic: PA & SS effects
  - Probit: PA & SS effects
  - Example: Crossover data (alcohol use)
- Ordinal Models
  - EDA
  - Extension of logistic regression (P.O. model)
  - Example: Schiz data (psychiatric drugs)

Multi-level Models: Review



Key Components of Multi-level Models

- Specification of predictor variables from multiple levels (fixed effects)
  - Variables to include
  - Key interactions
- Specification of correlation among responses from same clusters
  - Marginal (GEE)
  - Random (GLMM)
  - Transitional (Time-Series)
- Choices must be driven by scientific understanding, the research question and empirical evidence.

Digression on Statistical Models

- A statistical model is an approximation to reality
- There is not a “correct” model;
  - (forget the holy grail)
- A model is a tool for asking a scientific question;
  - (screw-driver vs. sludge-hammer)
- Useful models often combine the data with prior information to address the question of interest.
- Many models are better than one.

Multi-level Shmulti-level

- Multi-level analyses of social/behavioral phenomena: an important idea
- Multi-level models involve predictors from multiple-levels and their interactions
- They must account for associations among observations within clusters (levels) to make efficient and valid inferences.

Regression with Correlated Data

Must take account of correlation to:

- Obtain valid inferences
  - standard errors
  - confidence intervals
  - posteriors
- Make efficient inferences

Logistic Regression Example: Cross-over trial

Group	(1,1)	(0,1)	(1,0)	(0,0)	Total	1	2
AB	22	0	6	6	34	28	22
BA	18	4	2	9	33	20	22

- Response: 1-normal; 0- alcohol dependence
- Predictors: period (x_1); Placebo group (x_2)
- Two observations per person (cluster)
- Parameter of interest: log odds ratio of dependence: placebo vs treatment

Mean Model: $\log\{\text{odds}(AD)\} = \beta_0 + \beta_1 \text{Period} + \beta_2 \text{Pl}$

Marginal Models

- Focus is on the "mean model": E(Y|X)
- Group comparisons are of main interest
  - Treatment vs non-treatment
  - Exposure vs non-exposure
  - Demographic comparisons
- Within-cluster associations are accounted for to correct standard errors, but are not of main interest.

Marginal Model Interpretations

- log{ odds(AlcDep) } = $\beta_0 + \beta_1$Period + $\beta_2$pl

  = 0.67 + (-0.30)Period + (0.57)pl

TRT Effect: (placebo vs. trt)

OR = exp(0.57) = 1.77, 95% CI (1.12, 2.80)

⇨ *Risk of Alcohol Dependence is almost twice as high on placebo, regardless of, (adjusting for), time period*

WHY?

Since: log{odds(AlcDep|Period, pl)} = $\beta_0 + \beta_1$Period + β_2

And: log{odds(AlcDep|Period, trt)} = $\beta_0 + \beta_1$Period

Δ log-Odds = β_2

➡ OR = exp(β_2)

Random Effects Models

- Conditional on unobserved latent variables or "random effects"
  - Responses (Alcohol use) within a person over time are usually related, but the association is not the same for everyone (heterogeneity)
  - Alcohol use within a family is related because family members share an unobserved "family effect": common genes, diets, family culture and other unmeasured factors
  - Repeated observations within a neighborhood are correlated because neighbors share: common traditions, access to services, stress levels,…

Random Effects Model Interpretations

WHY?

Since: $\log\{\text{odds}(\text{AlcDep}_i|\text{Period}, \text{pl}, b_i)\} = \beta_0 + \beta_1\text{Period} + \beta_2 + b_i$

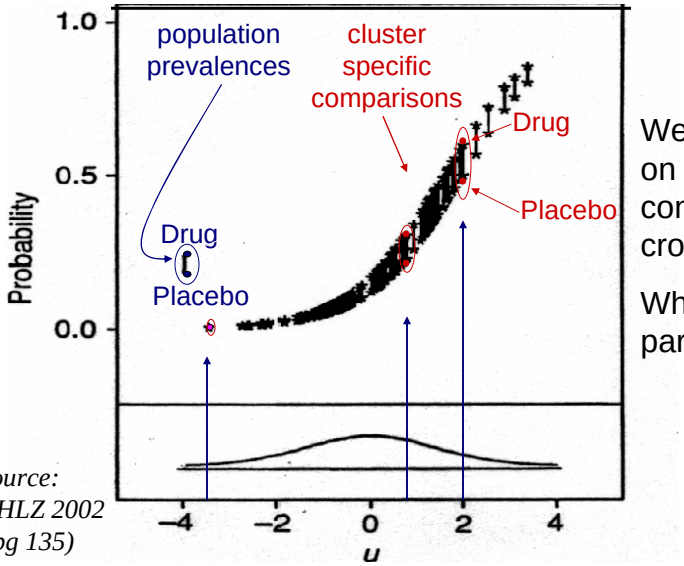
And: $\log\{\text{odds}(\text{AlcDep}|\text{Period}, \text{trt}, b_i)\} = \beta_0 + \beta_1\text{Period} + b_i$

Δ log-Odds = β_2

➡ OR = $\exp(\beta_2)$

- In order to make comparisons we must keep the subject-specific latent effect (b_i) the same.
- In a Cross-Over trial we have outcome data for each subject on both placebo & treatment
- In other study designs we may not.

Marginal –vs- Random Intercept Model



Source: DHLZ 2002 (pg 135)

We have evidence on the conditional contrast in a cross-over trial.

What about usual parallel RCTs?

Marginal vs. Random Effects Models

- For linear models, regression coefficients in random effects models and marginal models are identical:

  average of linear function = linear function of average

- For non-linear models, (logistic, log-linear,…) coefficients have different meanings/values, and address different questions
  - Marginal models -> *population-average* parameters
  - Random effects models -> cluster-*specific* parameters

Marginal -vs- Random Intercept Models; Cross-over Example

	Model		
Variable	Ordinary Logistic Regression	Marginal (GEE) Logistic Regression	Random-Effect Logistic Regression
Intercept	0.66 (0.32)	0.67 (0.29)	2.2 (1.0)
Period	-0.27 (0.38)	-0.30 (0.23)	-1.0 (0.84)
Treatment	0.56 (0.38)	0.57 (0.23)	1.8 (0.93)
Log OR (assoc.)	0.0	3.56 (0.81)	5.0 (2.3)

Comparison of Marginal and Random Effect Logistic Regressions

- Regression coefficients in the random effects model are roughly 3.3 times as large
  - Marginal: population odds (prevalence with/prevalence without) of AlcDep is exp(.57) = 1.8 greater for placebo than on active drug;
    population-average parameter
  - Random Effects: a person's odds of AlcDep is exp(1.8)= 6.0 times greater on placebo than on active drug;
    cluster-specific, here person-specific, parameter

Which model is better? They ask different questions.

Relationship between Marginal and RE models

$$P\left(y_{ij}=1 \mid x_1, x_2\right)$$

$$= \int P\left(y_{ij}=1 \mid x_1, x_2, \varsigma_i\right)\phi(\varsigma_i; 0, \hat{\tau}^2)d\varsigma_i$$

Normal density

We can obtain marginal probabilities from the individual level probabilities by integrating out the random effects

Marginalized Multilevel Models!

Probit Regression Example: Cross-over trial

- Response: 1-normal; 0- alcohol dependence
- Predictors:
  - period (x_1);
  - Placebo group (x_2)
- Two observations per person (cluster)
- Parameter of interest: log odds ratio of dependence: treatment vs placebo

Mean Model: $\Phi^{-1}\{\Pr(AD=1)\} = \beta_0 + \beta_1 \text{period} + \beta_2 \text{Pl}$

Marginal -vs- Random Intercept Models; Cross-over Probit Example

	Model		
Variable	Ordinary Probit Regression	Marginal (GEE) Probit Regression	Random-Effect Probit Regression
Intercept	0.61 (0.38)	0.60 (0.29)	1.38 (0.65)
Period	-0.18 (0.23)	-0.19 (0.14)	-0.45 (0.35)
Treatment	0.29 (0.23)	0.34 (0.14)	0.79 (0.37)
Log tau (assoc.)	0.0	"nuisance"	0.67 (0.18)

Marginalized Probit Model

$$P(y_{ij}=1 \mid x)$$

Normal density

$$= \int P(y_{ij}=1 \mid x, \varsigma_i)\phi(\varsigma_i;0,\tau^2)d\varsigma_i$$

$$= \int \Phi(x\beta+\varsigma_i)\phi(\varsigma_i;0,\tau^2)d\varsigma_i$$

$$= \Phi\left(\frac{x\beta}{\sqrt{1+\tau^2}}\right)$$

Closed Form Solution!

Marginal -vs- Random Intercept Models; Cross-over Probit Example

	Model			
Variable	Ordinary Probit Regression	Marginal (GEE) Probit Regression	Random-Effect Probit Regression	MMM $\frac{\beta^{RE}}{\sqrt{1+\tau^2}}$
Intercept	0.61 (0.38)	0.60 (0.29)	1.38 (0.65)	0.63
Period	-0.18 (0.23)	-0.19 (0.14)	-0.45 (0.35)	-0.20
Treatment	0.29 (0.23)	0.34 (0.14)	0.79 (0.37)	0.35
Log tau (assoc.)	0.0	"nuisance"	0.67 (0.18)	

Construct Contrasts of Interest

- RE model:
  - $\Phi^{-1}\{Pr(AD=1)\} = \beta_0 + \beta_1 period + \beta_2 Pl + \varsigma_i$
    - with: $\varsigma_i \sim N(0, \tau^2)$
  - $Pr(AD=1) = \Phi\{(\beta_0 + \beta_1 period + \beta_2 Pl) / \sqrt{(1+ \tau^2)}\}$
- Marginal RR(Pl vs trt, period 1)

  $= \Phi\{(\beta_0+ \beta_2) / \sqrt{(1+ \tau^2)}\} \ / \Phi\{\beta_0 / \sqrt{(1+ \tau^2)}\}$
- Marginal OR, etc…

Key Points

- "Multi-level" Models:
  - Have covariates from many levels and their interactions
  - Acknowledge correlation among observations from within a level (cluster)
- Assumptions about the latent variables determine the nature of the within cluster correlations
- Information can be borrowed across clusters (levels) to improve individual estimates
- Goal: Group Comparisons => Marginal Models
- Goal: Describe Heterogeneity => RE Models

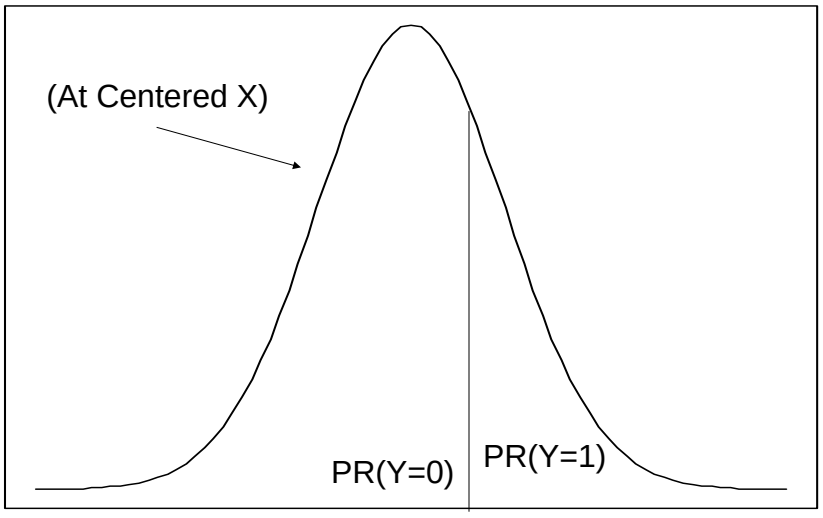
Marginalized Multilevel Models

- Allows group comparisons
- Allows description of heterogeneity
- Allows associations to be non-nuisance
- Full Likelihood (RE) model => MAR
- Best parts of all worlds

Ordinal Responses

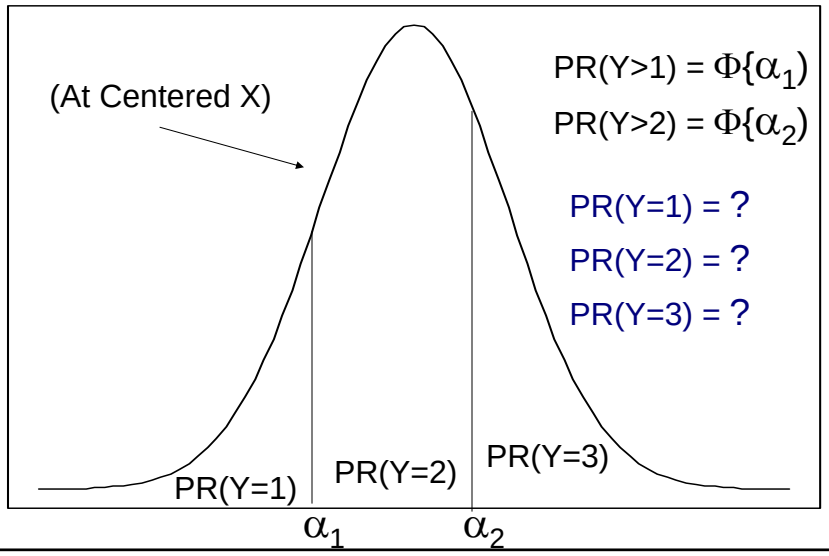
Latent Response (probit) form

Binary outcome: $\Phi^{-1}\{Pr(Y=1)\} = \beta_0 + X\beta$



Latent Response (probit) form

Ordinal outcome: $\Phi^{-1}\{Pr(Y>s)\} = \alpha_s + X\beta$



Cumulative Response Models

- Logistic regression: 2-categories (0/1)
  - $\log\{ Pr(Y=1) / [1-Pr(Y=1)] \} = \beta_0 + X\beta$
  - $\log\{ Pr(Y=1) / Pr(Y=0) \} = \beta_0 + X\beta$
  - $\log\{ Pr(Y>0) / Pr(Y\leq 0) \} = \beta_0 + X\beta$
- P.O. regression: S-categories (1,2,…,S)
  - $\log\{ Pr(Y>1) / Pr(Y\leq 1) \} = \alpha_1 + X\beta$
  - $\log\{ Pr(Y>2) / Pr(Y\leq 2) \} = \alpha_2 + X\beta$
  - $\log\{ Pr(Y>s) / Pr(Y\leq s) \} = \alpha_s + X\beta$
  - $\log\{ Pr(Y>s) / [1-Pr(Y>s)] \} = \alpha_s + X\beta$
- Note: Gllamm uses $-k_s$ for α_s

Ordered Responses

- Probit: $\Phi^{-1}\{Pr(Y>s)\} = \alpha_s + X\beta$
- PO: $\log\{odds(Y>s)\} = \alpha_s + X\beta$
- s = 1..(S-1) & check manuals for $-\alpha_s, -X\beta$
- Interpretations: β represents the assoc of a 1-unit increase in X with a change in logodds of being in ANY cumulative cat.
- Ex: 3-cat PO: $\log\{odds(Y>s)\} = \alpha_s + X\beta$, s=1,2
  - $logodds(Y>1) = \alpha_1 + X\beta$
  - $logodds(Y>2) = \alpha_2 + X\beta$

Strong Assumption

Schiz Data:

Schizophrenia Collaborative Study (NIMH)

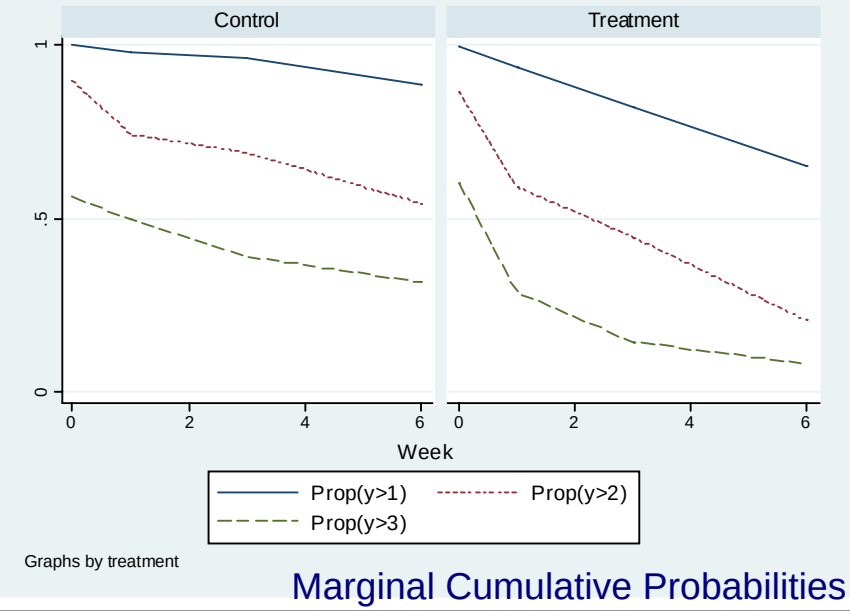
- Antipsychotic Drugs & Schiz. Severity
- 437 patients
  - Placebo (0) & treatment (1)
  - Trt = (Chlorpromazine, Fluphenazine, or Thioridazine)
- 7 potential visits for each patient (0..6)
- Outcome: IMPS item 79
  - Inpatient Multidimensional Psychiatric Scale
  - 1=Normal, 2=mildly ill, 3=markedly ill, 4=severely
- Q1) How well does trt work vs Placebo?
- Q2) How variable are patients' responses

Schiz Data cont: Data Patterns

Freq.	Percent	Cum.	Pattern
308	70.48	70.48	11.1..1
41	9.38	79.86	11.1...
37	8.47	88.33	11.....
8	1.83	90.16	11....1
8	1.83	91.99	111....
6	1.37	93.36	11.1.1.
5	1.14	94.51	1..1..1
5	1.14	95.65	11.11..
3	0.69	96.34	.1.1..1
16	3.66	100.0	(other patterns)
437	100.00		XXXXXXX

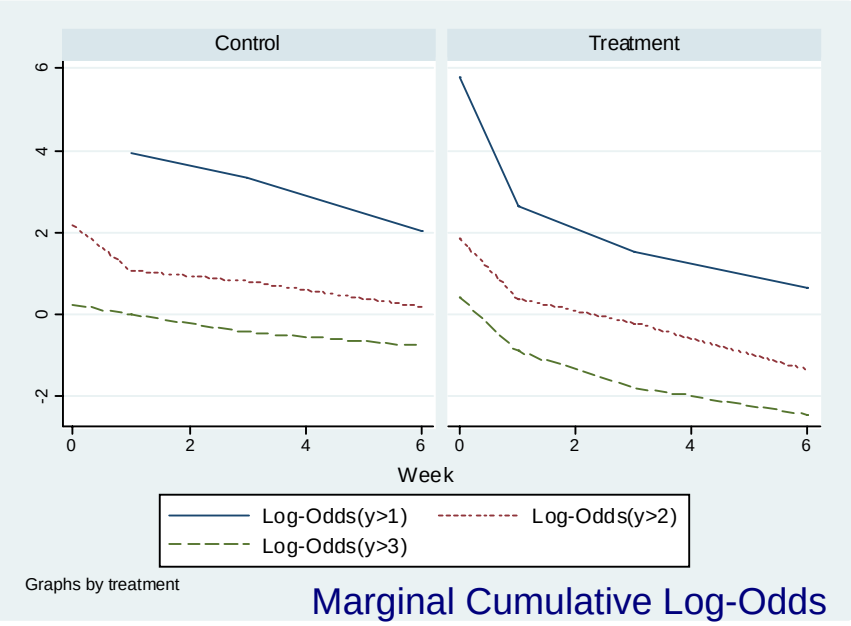
week	treatment 0	1	Total
0	107	327	434
1	105	321	426
2	5	9	14
3	87	287	374
4	2	9	11
5	2	7	9
6	70	265	335

Cumulative Probabilities over Weeks



Marginal Cumulative Probabilities

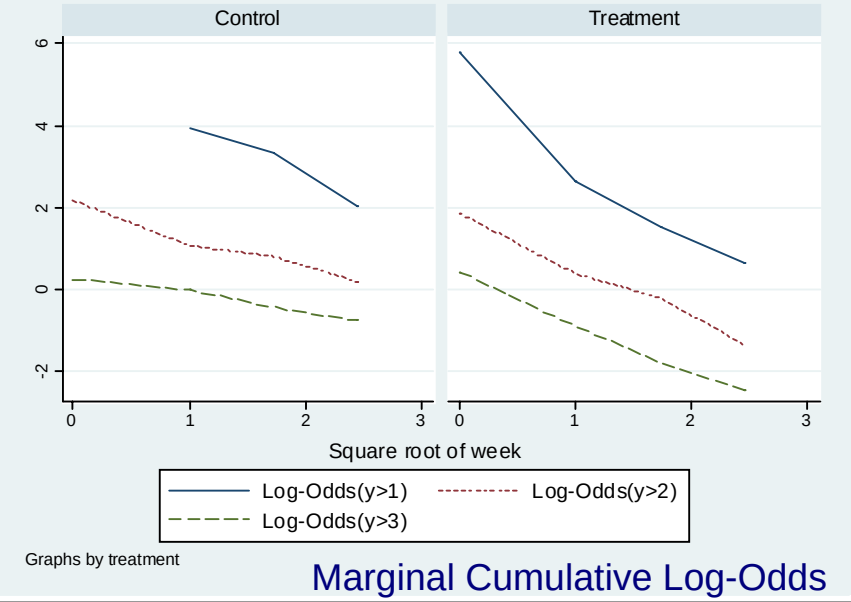
Cumulative Log-Odds over Weeks



Graphs by treatment

Marginal Cumulative Log-Odds

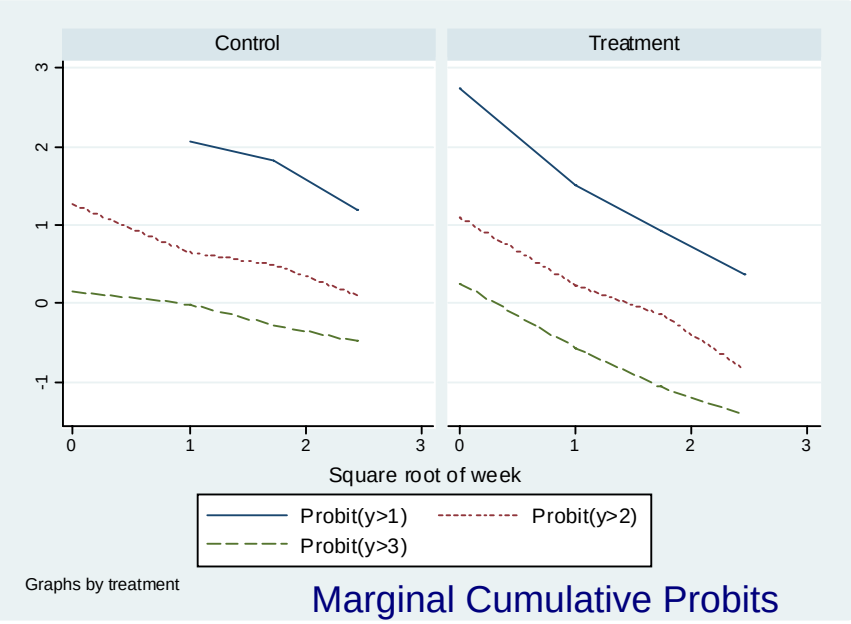
Cumulative Log-Odds over √weeks



Graphs by treatment

Marginal Cumulative Log-Odds

Cumulative Probits over √weeks



Marginal Cumulative Probits

Ordinary P.O. model: stata

```
ologit impso weeksqrt treatment interact,
                    or robust cluster(id)

Ordered logistic regression                     Number of obs   =       1603
                                                Wald chi2(3)    =     440.17
                                                Prob > chi2     =     0.0000
Log pseudolikelihood = -1878.0969               Pseudo R2       =     0.1177

                                (Std. Err. adjusted for 437 clusters in id)
------------------------------------------------------------------------------
             |               Robust
        impso | Odds Ratio   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
    weeksqrt |   .5847056   .0591797    -5.30   0.000     .4794958    .7130004
   treatment |   .9993959   .2042595    -0.00   0.998     .6695244    1.491793
    interact |   .4719089   .0568135    -6.24   0.000     .3727189    .5974961
-------------+----------------------------------------------------------------
       /cut1 |  -3.807279   .1956796                     -4.190804   -3.423754
       /cut2 |  -1.760167   .1811041                     -2.115125    -1.40521
       /cut3 |  -.4221112   .1795596                     -.7740415   -.0701808
------------------------------------------------------------------------------
```

Ordinary PO interpretations

Model: $\log\{\text{odds}(Y>s)\} = \alpha_s + \beta_1 \text{swk} + \beta_2 \text{trt} + \beta_3 \text{swk*trt}$

- $\log\{\text{odds}(Y>1 \mid \text{wk}=0, \text{trt})\} = \alpha_1 + \beta_2$
- $\log\{\text{odds}(Y>1 \mid \text{wk}=0, \text{Pl})\} = \alpha_1$

$\exp(\beta_2) = 1.0$

- $\log\{\text{odds}(Y>2 \mid \text{wk}=0, \text{trt})\} = \alpha_2 + \beta_2$
- $\log\{\text{odds}(Y>2 \mid \text{wk}=0, \text{Pl})\} = \alpha_2$

$\exp(\beta_2) = 1.0$

- Effects are the same across cumulative cats
- No effect at baseline

Ordinary PO interpretations

Model: $\log\{\text{odds}(Y>s)\} = \alpha_s + \beta_1 \text{swk} + \beta_2 \text{trt} + \beta_3 \text{swk*trt}$

- $\log\{\text{odds}(Y>1 \mid \text{wk}=1, \text{trt})\} = \alpha_1 + \beta_1 + \beta_2 + \beta_3$
- $\log\{\text{odds}(Y>1 \mid \text{wk}=1, \text{Pl})\} = \alpha_1 + \beta_1$

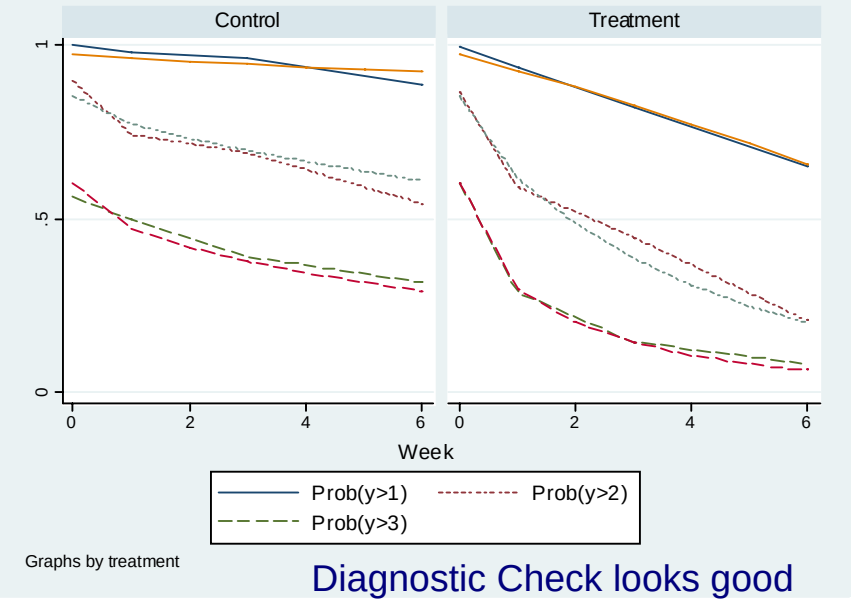
$\exp(\beta_2+\beta_3) = 0.28$

- $\log\{\text{odds}(Y>2 \mid \text{wk}=1, \text{trt})\} = \alpha_1 + \beta_1 + \beta_2 + \beta_3$
- $\log\{\text{odds}(Y>2 \mid \text{wk}=1, \text{Pl})\} = \alpha_1 + \beta_1$

$\exp(\beta_2+\beta_3) = 0.28$

- Effects are the same across cumulative cats
- 72% Reduction in “risk” (odds) at wk1, trt vs pl

Observed & Predicted Probs



Diagnostic Check looks good

Ordered Responses w/ Ran Ints

- Probit: $\Phi^{-1}\{Pr(Y>s)\} = \alpha_s + X\beta + u_i$
- PO: $\log\{odds(Y>s)\} = \alpha_s + X\beta + u_i$
- s = 1..(S-1) & check manuals for $-\alpha_s$, $-X\beta$
- Interpretations: β represents the assoc of a 1-unit increase in X with a change in logodds of being in ANY cumulative cat. *for a single patient.*
- Ex: 3-cat PO: $\log\{odds(Y>s)\} = \alpha_s + X\beta + u_i$, s=1,2
  - $\log odds(Y>1) = \alpha_1 + X\beta + u_i$
  - $\log odds(Y>2) = \alpha_2 + X\beta + u_i$

Strong Assumption

Ran Int P.O. model: gllamm

```
gllamm impso weeksqrt treatment interact,
     i(id) link(ologit) adapt eform
```

```
------------------------------------------------------------------------------
       impso |     exp(b)   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
impso        |
    weeksqrt |   .4649525   .0608031    -5.86   0.000     .3598277    .6007899
   treatment |   .9439404   .2962807    -0.18   0.854     .5102375    1.746291
    interact |   .2993646   .0457031    -7.90   0.000     .2219474    .4037855
-------------+----------------------------------------------------------------
_cut11       |  -5.858453    .331792   -17.66   0.000    -6.508753   -5.208153
-------------+----------------------------------------------------------------
_cut12       |  -2.825669   .2900513    -9.74   0.000    -3.394159   -2.257179
-------------+----------------------------------------------------------------
_cut13       |  -.7077072   .2750904    -2.57   0.010    -1.246875   -.1685399
------------------------------------------------------------------------------
 Variances and covariances of random effects
------------------------------------------------------------------------------
***level 2 (id)
    var(1): 3.7733416 (.46496878)
------------------------------------------------------------------------------
```

Ran. Int. (SS) PO interpretations

Model: $\log\{\text{odds}(Y>s)\} = \alpha_s+\beta_1 swk+\beta_2 trt+\beta_3 swk*trt+ u_i$

- $\log\{\text{odds}(Y>1 \mid wk=0, trt)\} = \alpha_1 + \beta_2 + u_i$
- $\log\{\text{odds}(Y>1 \mid wk=0, Pl)\} = \alpha_1 + u_i$

$\exp(\beta_2)= 0.94$

- $\log\{\text{odds}(Y>2 \mid wk=0, trt)\} = \alpha_2 + \beta_2$
- $\log\{\text{odds}(Y>2 \mid wk=0, Pl)\} = \alpha_2$

$\exp(\beta_2)= 0.94$

- At baseline, no effect comparing a single patient on trt, to that same patient off trt??

Ran. Int. (SS) PO interpretations

Model: $\log\{\text{odds}(Y>s)\} = \alpha_s+\beta_1 swk+\beta_2 trt+\beta_3 swk*trt+ u_i$

- $\log\{\text{odds}(Y>1 \mid wk=1, trt)\} = \alpha_1 + \beta_1+ \beta_2+ \beta_3 + u_i$
- $\log\{\text{odds}(Y>1 \mid wk=1, Pl)\} = \alpha_1 + \beta_1 \quad + u_i$

$\exp(\beta_2+\beta_3)= 0.14$

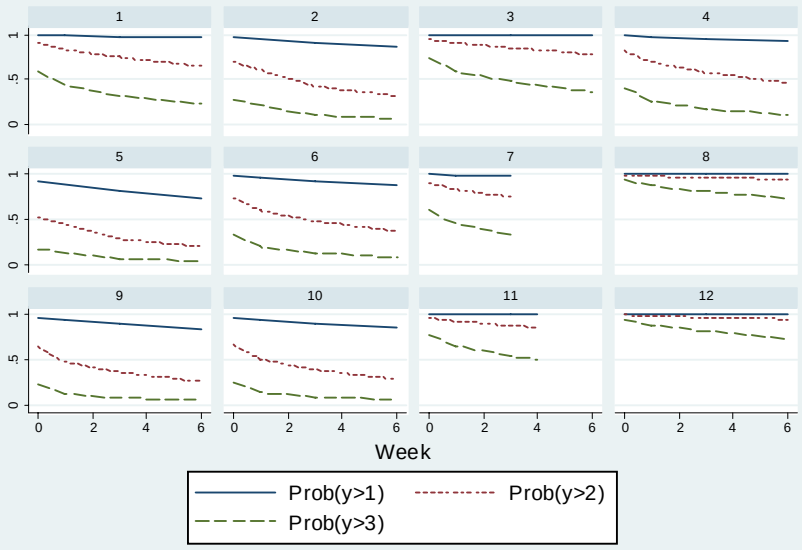
- Similar at week 1, etc. The SS trt effect compares a single patient on trt, to that same patient off trt but we have not observed any actual data on this effect. This is a "causal extrapolation"

How Heterogeneous is the data?

Model: $\log\{\text{odds}(Y>s)\} =\alpha_s+\beta_1 swk+\beta_2 trt+\beta_3 swk*trt+ u_i$

- If a patient is on trt (or off), how variable is their specific outcome trajectory?
- Estimate of Ran Int variance: 3.77 (0.46)
- Huge!
- Can we visualize?
- Sure, use Empirical Bayes estimates of u_i

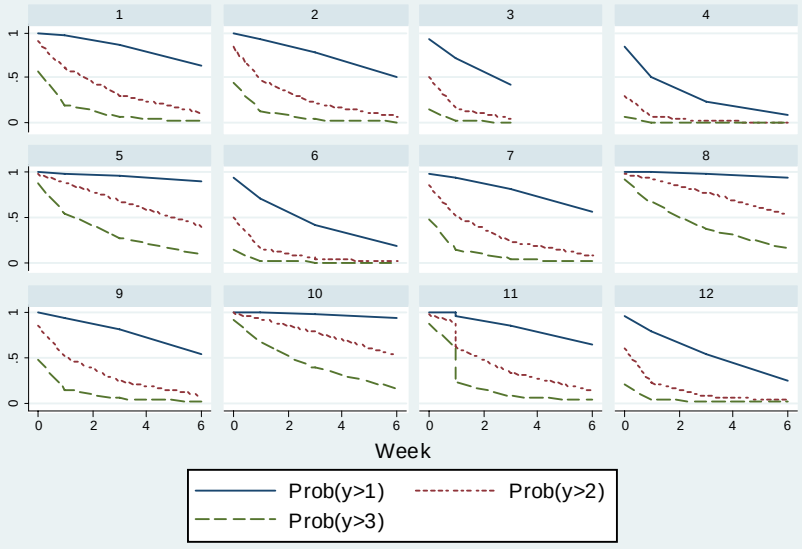
Patient-Specific Trajectories



Graphs by newid

Placebo

Patient-Specific Trajectories



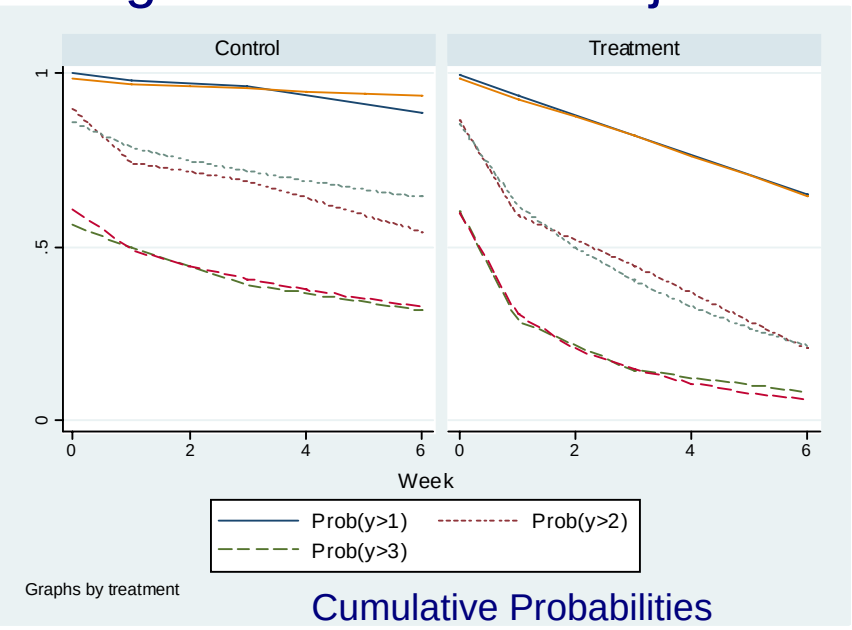
Graphs by newid

Treatment

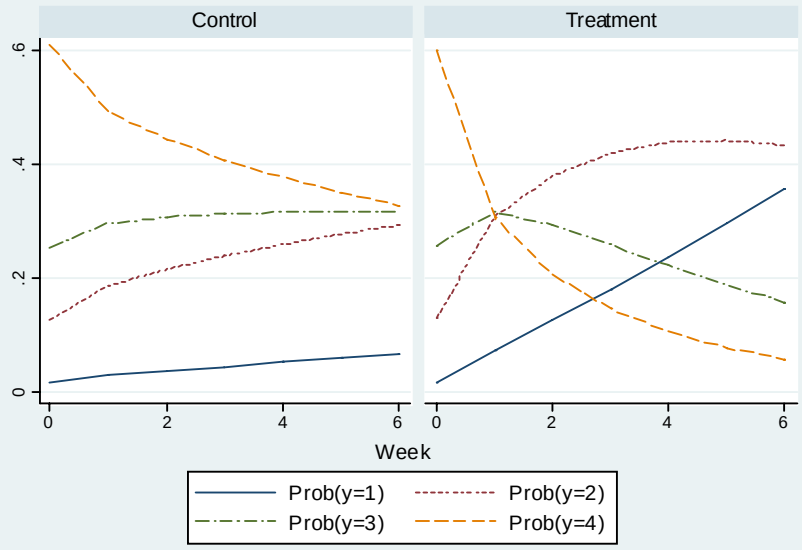
Can we Marginalize the PO model?

- Of course, the marginalized version integrates the random effects out over their assumed distribution
- no more causal extrapolation
- Currently not implemented in Stata, but see *"A User Friendly Guide to Link-Probit Models"* – Caffo, Griswold; TAS 2006
- We can use Gllamm's post-estimation prediction to compute the marginal probabilities for visualization however…

Marginal Cum. Prob.Trajectories



Marginal Prob.Trajectories



Ordinal Category Probabilities

Relaxing the PO assumption

- PO: $\log\{\text{odds}(Y>s)\} = \alpha_s + X\beta$
- Non-PO: $\log\{\text{odds}(Y>s)\} = \alpha_s + X\beta_s$
- s = 1..(S-1) & check manuals for $-\alpha_s$, $-X\beta_s$
- Interpretations: β_s represents the assoc of a 1-unit increase in X with a change in logodds of being in cumulative cat. "s"
- Ex: 3-cat PO: $\log\{\text{odds}(Y>s)\} = \alpha_s + X\beta_s$, s=1,2
  - $\text{logodds}(Y>1) = \alpha_1 + X\beta_{11}$
  - $\text{logodds}(Y>2) = \alpha_2 + X\beta_{21}$

Relaxed Assumption

non-P.O. model: gologit

```
gologit impso weeksqrt treatment interact, cluster(id) robust
```

(Std. Err. adjusted for 437 clusters in id)

impso	Odds Ratio	Robust Std. Err.	z	P>|z|	[95% Conf.	Interval]
mleq1						
weeksqrt	.2041182	.0937231	-3.46	0.001	.0829934	.5020189
treatment	.1793261	.1833936	-1.68	0.093	.0241621	1.330921
interact	1.054759	.5020053	0.11	0.911	.4149823	2.680876
mleq2						
weeksqrt	.4847473	.0609446	-5.76	0.000	.3788772	.6202008
treatment	.7877922	.2234486	-0.84	0.400	.4518327	1.373554
interact	.5892814	.0865812	-3.60	0.000	.4418333	.7859357
mleq3						
weeksqrt	.66977	.069234	-3.88	0.000	.5469368	.8201896
treatment	1.061012	.2399695	0.26	0.793	.6810892	1.652863
interact	.441081	.0588683	-6.13	0.000	.3395579	.5729581
_cons1	5.986731	.9860904	6.07	0.000	4.05403	7.919433
_cons2	1.996487	.2504722	7.97	0.000	1.505571	2.487404
_cons3	.30472	.1993504	1.53	0.126	-.0859997	.6954397

Compare w/ P.O. model: ologit

```
ologit impso weeksqrt treatment interact,
                or robust cluster(id)
```

```
Ordered logistic regression                     Number of obs   =       1603
                                                Wald chi2(3)    =     440.17
                                                Prob > chi2     =     0.0000
Log pseudolikelihood = -1878.0969               Pseudo R2       =     0.1177
```

(Std. Err. adjusted for 437 clusters in id)

impso	Odds Ratio	Robust Std. Err.	z	P>|z|	[95% Conf.	Interval]
weeksqrt	.5847056	.0591797	-5.30	0.000	.4794958	.7130004
treatment	.9993959	.2042595	-0.00	0.998	.6695244	1.491793
interact	.4719089	.0568135	-6.24	0.000	.3727189	.5974961
/cut1	-3.807279	.1956796			-4.190804	-3.423754
/cut2	-1.760167	.1811041			-2.115125	-1.40521
/cut3	-.4221112	.1795596			-.7740415	-.0701808

Relaxing the PO assumption

- PO: $\log\{\text{odds}(Y>s)\} = \alpha_s + X\beta + u_i$
- Non-PO: $\log\{\text{odds}(Y>s)\} = \alpha_s + X\beta_s + u_i$
- s = 1..(S-1) & check manuals for $-\alpha_s$, $-X\beta_s$
- Interpretations: β_s represents the assoc of a 1-unit increase in X with a change in logodds of being in cumulative cat. "s" *for a single patient.*
- Ex: 3-cat PO: $\log\{\text{odds}(Y>s)\} = \alpha_s + X\beta + u_i$, s=1,2
  - $\text{logodds}(Y>1) = \alpha_1 + X\beta_1 + u_i$
  - $\text{logodds}(Y>2) = \alpha_2 + X\beta_2 + u_i$

Strong Assumption

Ran. Int. (SS) non-PO interpretations

$\log\{\text{odds}(Y>s)\} = \alpha_s + \beta_{s1}\text{swk} + \beta_{s2}\text{trt} + \beta_{s3}\text{swk*trt} + u_i$

- $\log\{\text{odds}(Y>1 \mid \text{wk}=0, \text{trt})\} = \alpha_1 + \beta_{12} + u_i$
- $\log\{\text{odds}(Y>1 \mid \text{wk}=0, \text{Pl})\} = \alpha_1 + u_i$

$\exp(\beta_{12}) = ??$

- $\log\{\text{odds}(Y>2 \mid \text{wk}=0, \text{trt})\} = \alpha_2 + \beta_{22}$
- $\log\{\text{odds}(Y>2 \mid \text{wk}=0, \text{Pl})\} = \alpha_2$

$\exp(\beta_{22}) = ??$

- Gllamm still running…

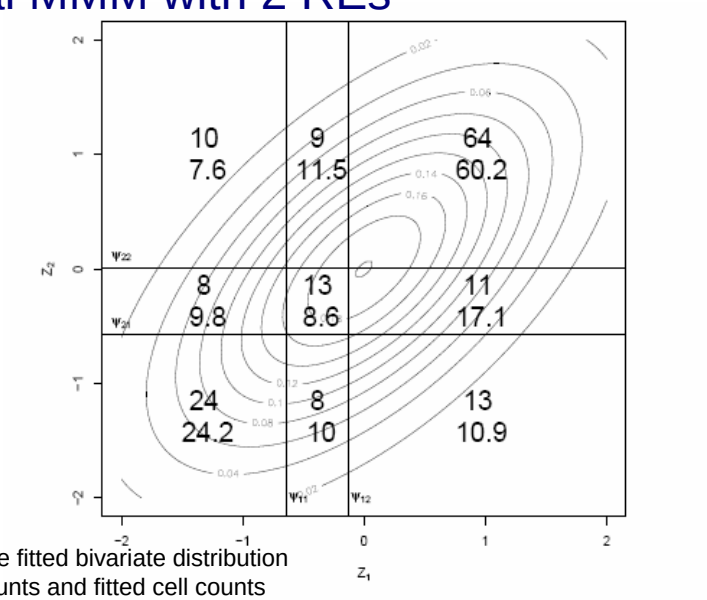
Schiz Summary

- Under a common trt effect, general 72% decrease in cumulative odds risk per unit time (sqrt week).
- Patient responses are highly variable, so the marginal responses may not fit an individual's response well.
- Could model this with MMM (probit) to handle both estimation aspects
- Potentially less change over time in lower categories
- Potentially stronger trt effects in upper categories

Ordinal MLM notes

- PO models are basically logistic regressions
  - popular
  - strong parallel regression assumption
  - Can be relaxed
- Mixed PO have SS, not PA effects (from logit)
- Other models:
  - Ordinal Probit
  - Continuation ratio model
  - Multinomial logit model
- Additional REs (random slopes, etc.)

From Caffo & Griswold TAS 2006: Ordinal MMM with 2 REs



Contour plot of the fitted bivariate distribution along with cell counts and fitted cell counts

Overall Summary: MLMs

- Powerful tools / dangerous black boxes
- "Buyer Beware"
  - Model Assumptions: both fixed AND random ($u_i \sim N(0,\tau^2)$)
  - Identifiability
  - Model Fit: Marginalize & Check whenever possible
  - Report Heterogeneity as well (& meaning)
  - MLMs require even more due-diligence than usual
- Marginal Models (~GEE)
  - Nice PA interpretations, more robust
- RE models (~GLMM)
  - Nice MAR, flexible assoc, full likelihood
- MMM: best of both worlds