A Gentle Introduction to Generalized Linear Mixed Models

Dr. Isabella Ghement for

THE ANALYSIS FACTOR

Motivation

Generalized **L**inear **M**ixed **E**ffects **M**odels
(**GLMM**s)

GLMMs are a tough nut to crack.

Why?

2

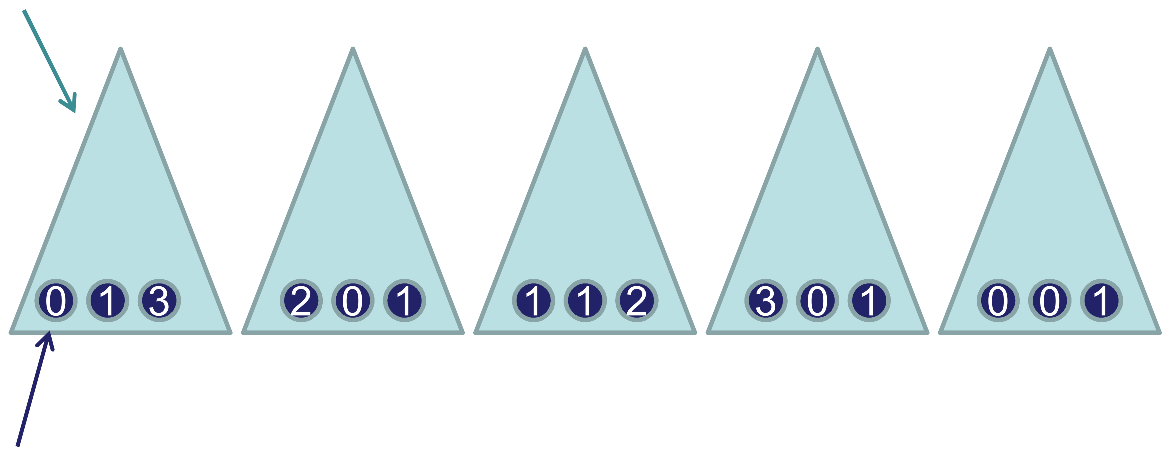
What are GLMMs?

GLMMs are regression models
for 'grouped' non-normal response data,
which include 'fixed' and 'random' effects.

Example

Rehab center (randomly selected from a population of centers)

Rehab center is a 'grouping' variable.
Cardiac patients are 'nested' in rehab centers.



Cardiac patient with 0 incidents

Response: Incidents (i.e., number of cardiac incidents for a patient over 6 months)
Patient-Level Predictors: Treatment (Standard vs. New)
Center-Level Predictor: Hours (i.e., number of hours center is open to cardiac patients each week)

Audience

Can you give one other example of ‘groups’ and ‘individuals’?

Can you give an example of non-normal response variable you would collect on the ‘individuals’ in the proposed ‘groups’?

Can you give examples of group-level and individual-level predictors?

5

Why use GLMMs?

Separate

Analyze the data for each 'group' separately.

Lump

Lump the data from all 'groups' together, essentially ignoring the 'grouping'.

GLMMs provide a balance between two extremes: separating and lumping.

Audience

What do you think might be problematic about analyzing the data from each ‘group’ separately?

What do you think might be problematic about analyzing the lumped data from all ‘groups’?

When are GLMMs useful?

One possible setting:

When we are trying to determine how a number of individual-level and group-level predictor variables influence an individual-level response variable.

8

Audience

Can you think of other settings where GLMMs might be useful?

9

Random vs. Fixed Effects

GLMMs can include both ***fixed*** and ***random*** effects.

While this provides flexibility, it can lead to confusion about what fixed and random effects are, when we should include them in a GLMM, and in what form.

10

Random vs. Fixed Effects

Random Effects

- 'Grouping' variable
- Lower-level predictor variables

Fixed Effects

- Lower-level predictor variables
- Higher-level predictor variables

Effects are associated with variables.

11

Audience

Going back to our initial example, can you tell what type of effects might each of these variables have on the response variable incidents?

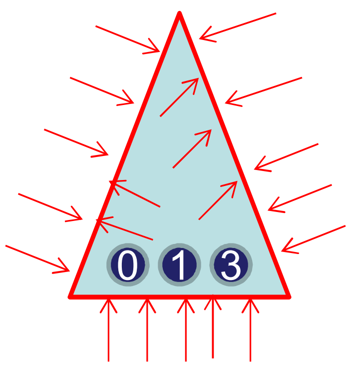
- Rehab center ('grouping' variable)
- Treatment (individual-level predictor)
- Hours (group-level predictor)

12

Random Group Effects

At a minimum, GLMMs include **random group effects (or random intercept effects)** for the 'grouping' variable(s) present in the data.

Thus, we can think of a 'grouping' variable as a **random factor**.



Random group (or intercept) effects capture group-level influences unaccounted for in the model that lead to within-group dependencies and between-group variation in the response data.

Often, each individual influence is small, but their combined effect can be sizeable.

13

Random Factor Interpretations

A random factor has two complementary interpretations.

Frequentist Interpretation

Can be problematic in practice.

Bayesian Interpretation

Can be more encompassing in practice.

14

Random Factor: Frequentist Interpretation

If we treat a 'grouping' variable as a random factor, we assume that **its values were chosen at random from a larger population of values**.

1. We can generalize our findings to group values that were NOT included in our study.

2. We can estimate the between-group variability across ALL groups.

Random Factor: Bayesian Interpretation

If we treat a 'grouping' variable as a random factor, we assume that:

1. One value of the factor can tell us something about other values.

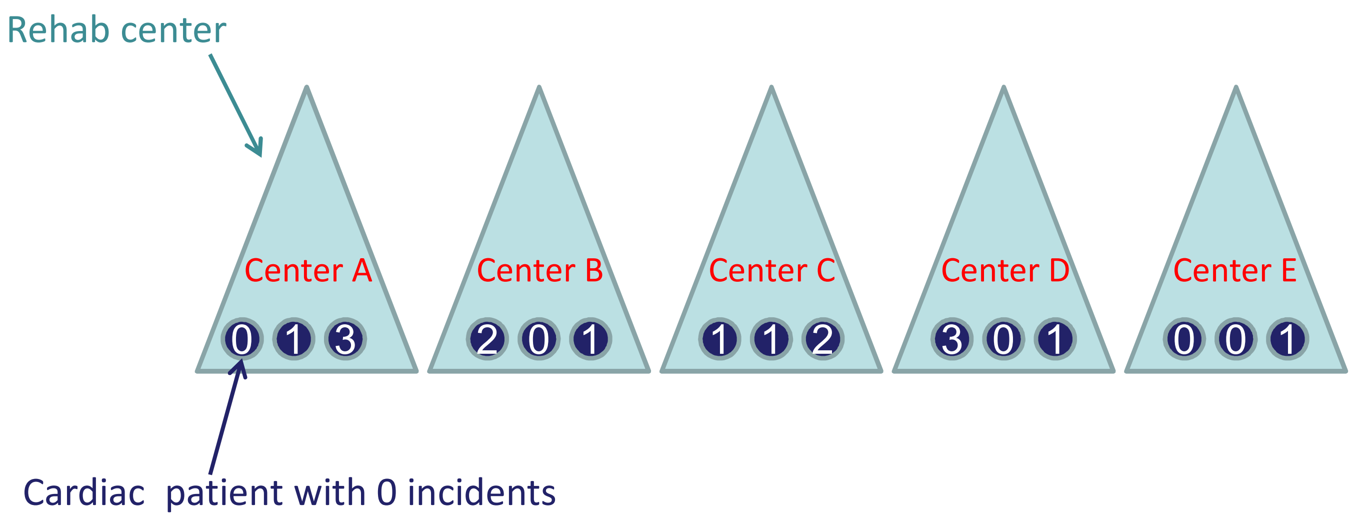
2. We can combine information across the different values of the factor.

16

Fixed vs. Random Effects for 'Grouping' Variable?

Can you ignore the labeling of the 'grouping' variable and still answer your research questions?

YES → Random Effects
NO → Fixed Effects



Response: Incidents (i.e., number of cardiac incidents for a patient over 6 months)
Patient-Level Predictor: Treatment (Standard vs. New)
Center-Level Predictor: Hours (i.e., number of hours center is open to cardiac patients each week)

17

Example of Poisson Regression Model with Random Group Effects and No Predictors

$$Incidents_{ij} \sim Poisson(\mu_{ij})$$

$$\log(\mu_{ij}) = \beta_{00} + u_{0j}$$

$$u_{0j} \sim Normal(0, \sigma_{00}^2)$$

$j - reserved\ for\ group$

$i - reserved\ for\ individual$

The null model provides a baseline against which we can compare more complex models.

Example of Poisson Regression Model with Fixed Group Effects and No Other Predictors

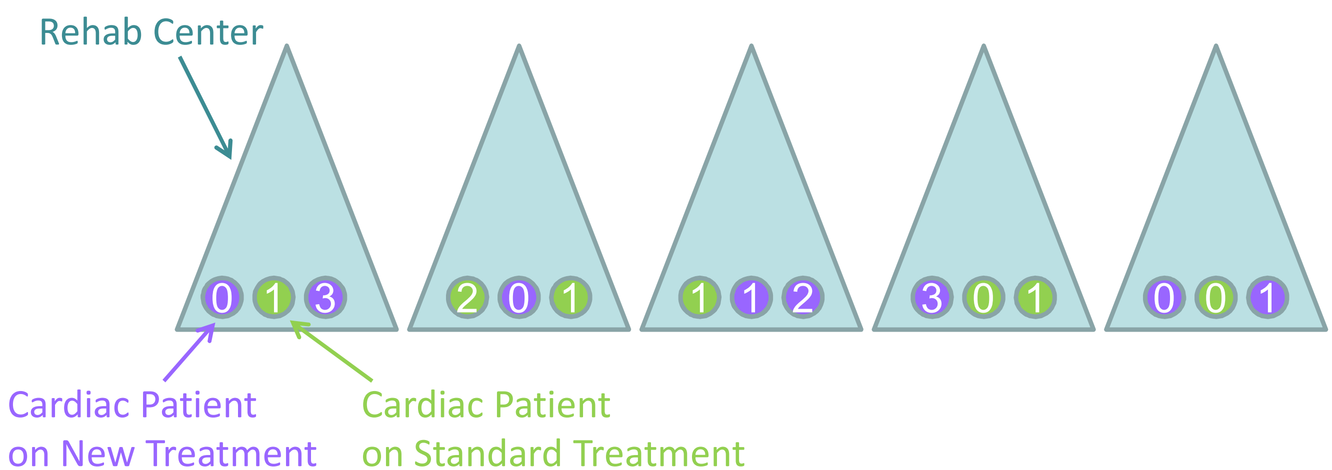
$$Incidents_{ij} \sim Poisson(\mu_{ij})$$

$$\log(\mu_{ij}) = \beta_0 + \beta_1 G_{1j} + \beta_2 G_{2j} + \beta_3 G_{3j} + \beta_4 G_{4j}$$

- Assume 5 groups (1,2,3,4,5)
- Treat last group as a reference
- Use 4 dummy variables to capture differences between non-reference and reference groups:
  - G1: 1 vs 5
  - G2: 2 vs 5
  - G3: 3 vs 5
  - G4: 4 vs 5

Random vs. Fixed Lower-Level Predictor Effects

Effect of Treatment in Each Group:
"Difference" in number of cardiac incidents between patients on New Treatment and those on Standard Treatment expressed on a multiplicative scale



Effect of Treatment is 'fixed': Same Treatment effect is assumed across ALL groups represented by the groups in the study

Effect of Treatment is 'random': Different Treatment effects are assumed across ALL groups represented by the groups in the study

20

Example of Poisson Regression Model with Random Group Effects and Fixed Effects of Lower-Level Predictor

$$Incidents_{ij} \sim Poisson(\mu_{ij})$$

$$\log(\mu_{ij}) = (\beta_{00} + u_{0j}) + \beta_{10} Treatment_{ij}$$

$$u_{0j} \sim Normal(0, \sigma_{00}^2)$$

β_{10} Effect of Treatment on the response variable after adjusting for (or holding constant) the ‘group’ effects

Example of Poisson Regression Model with Random Group Effects and Random Effects of Lower-Level Predictor

$$Incidents_{ij} \sim Poisson(\mu_{ij})$$

$$\log(\mu_{ij}) = \underbrace{(\beta_{00} + u_{0j})} + \underbrace{(\beta_{10} + u_{1j})} Treatment_{ij}$$

$$\begin{pmatrix} u_{0j} \\ u_{1j} \end{pmatrix} \sim MVN\left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_{00}^2 & \sigma_{01} \\ \sigma_{01} & \sigma_{11}^2 \end{pmatrix}\right)$$

Example of Poisson Regression Model with Random Group Effects, Random Effects of Lower-Level Predictor and Fixed Effects of Higher-Level Predictor

$$Incidents_{ij} \sim Poisson(\mu_{ij})$$

$$\log(\mu_{ij}) = (\beta_{00} + \beta_{01} Hours_j + u_{0j}) + (\beta_{10} + u_{1j}) Treatment_{ij}$$

Hours predictor helps explain some of the variability in the random intercepts.

No cross-level interaction between Hours and Treatment
(i.e., Hours predictor does NOT moderate the Treatment effect).

23

Example of Poisson Regression Model with Random Group Effects, Random Effects of Lower-Level Predictor and Fixed Effects of Higher-Level Predictor

$$Incidents_{ij} \sim Poisson(\mu_{ij})$$

$$\log(\mu_{ij}) = (\beta_{00} + \beta_{01} Hours_j + u_{0j}) + (\beta_{10} + \beta_{11} Hours_j + u_{1j}) Treatment_{ij}$$

Hours predictor helps explain some of the variability in the random intercepts and some of the variability in the random slopes associated with Treatment.

Cross-level interaction between Hours and Treatment (i.e., Hours predictor moderates the Treatment effect).

Audience

How would you describe the effect of Hours on Treatment for the previous model to someone else?

GLMM Estimation

Frequentist Methods:

- Direct Maximum Likelihood via Numerical Integration (R, SAS, STATA)
- Quasi-Likelihood Methods (SPSS, MLwiN, HLM)

Bayesian Methods:

- Marko Chain Monte Carlo (MCMC)

GLMM Interpretation

GLMM interpretation refers to the interpretation of the:

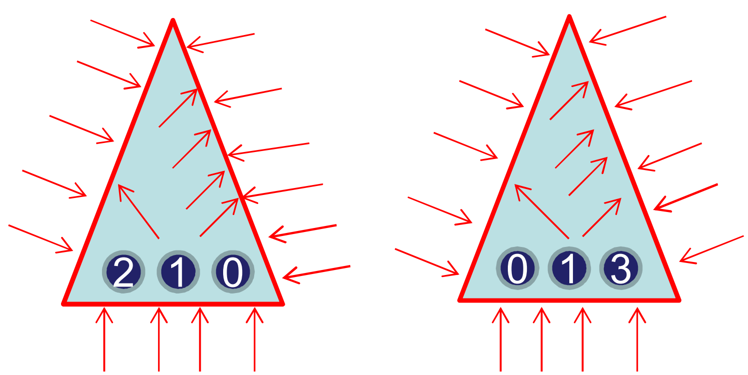
1. Estimated fixed effects;
2. Estimated variances/covariances of the random effects

27

GLMM Interpretation

Interpretation of the estimated fixed effects is **conditional** on the random effects and all other predictor variables included in the model.

See: http://www.ats.ucla.edu/stat/mult_pkg/glmm.htm



Random group (or intercept) effects capture unaccounted-for group-level influences that lead to within-group dependencies and between-group variation in the response data.

Interpreting variances of the random effects when designing a follow-up study

Random-effect variance is **low**	Random-effect variance is **high**
Not important to collect information on group-level predictors, as there is little potential that they explain group-level variance	Important to collect information on group-level predictors, as there is great potential that they explain group-level variance

29

Example of Random Intercept Poisson Regression with Two Lower-Level Predictors

$$Incidents \sim Poisson(\mu_{ij})$$

$$\log(\mu_{ij}) = \beta_{00} + \beta_{10} Treatment_{ij} + \beta_{20} Gender_{ij} + u_{0j}$$

$$u_{0j} \sim Normal(0, \sigma_{00}^2)$$

Example of Random Intercept Poisson Regression with Two Lower-Level Predictors

```
Fixed effects:
                        Estimate Std. Error z value Pr(>|z|)
(Intercept)     β̂00  0.78743    0.11394   6.911 4.81e-12
Treat           β̂10 -0.31172    0.03287  -9.484  < 2e-16 ***
Gender          β̂20  0.36044    0.03332  10.818  < 2e-16 ***
```

Significant Negative Relationship between Heart and Treatment:
Among patients of the same gender from the same rehab facility (or with the same random effect for rehab facility), **there are fewer cardiac warning incidents on average over 6 months for those in the treatment group than those in the control group.**

Significant Positive Relationship between Heart and Gender:
Among patients on the same treatment from the same rehab facility (or with the same random effect for rehab facility), **males experience more cardiac warnings signs on average over 6 months than females.**

31

Example of Random Intercept Poisson Regression with Two Lower-Level Predictors

```
> summary(model.1)
Generalized linear mixed model fit by maximum
likelihood (Laplace Approximation)

     AIC      BIC   logLik deviance df.resid
 11564.0  11583.6  -5778.0  11556.0      996

Random effects:
 Groups Name                 Variance Std.Dev.
 rehab  (Intercept)          1.263    1.124
Number of obs: 1000, groups:  rehab, 110
```

$\hat{\sigma}_{00}^2$

The expected number of cardiac warning incidents **for each treatment and gender condition combination** varies across rehabilitation centers.

32

Example of Random Intercept Poisson Regression with Lower-Level and Higher-Level Predictors

$$Incidents \sim Poisson(\mu_{ij})$$

$$\log(\mu_{ij}) = \beta_{00} + \beta_{10} Treatment_{ij} + \beta_{20} Gender_{ij} + \beta_{30} Hours_j + u_{0j}$$

$$u_{0j} \sim Normal(0, \sigma_{00}^2)$$

Example of Random Intercept Poisson Regression with Lower-Level and Higher-Level Predictors

Fixed effects:

		Estimate	Std. Error	z value	Pr(>|z|)	
(Intercept)	$\hat{\beta}_{00}$	-0.40933	0.46898	-0.873	0.38278	
Treatment	$\hat{\beta}_{10}$	-0.31192	0.03287	-9.491	< 2e-16	***
Gender	$\hat{\beta}_{20}$	0.36029	0.03332	10.813	< 2e-16	***
Hours	$\hat{\beta}_{30}$	0.28809	0.10916	2.639	0.00831	**

Significant Positive Relationship between Heart and Hours:

When comparing rehab facilities with the same random effect (i.e., sharing the same unobservable group-level characteristics), the more hours a rehab facility is open, the fewer warning signs same-gender patients on the same treatment will experience over a 6-month period.

GLMM Inference

For Direct Maximum Likelihood Methods:

- Wald-Tests
- Likelihood ratio tests
- AIC

GLMM Prediction

Complicated by the presence of random effects in the model.

Can be done by setting the random effects to zero or by averaging across (simulated/observed) random effects.

36

GLMM Model Building

Model building involves deciding what fixed and random effects to include in a GLMM model and in what form.

Top-Down

Complex model → **Trim it down**

Bottom-Up

Simple model → **Build it up**

Given the computational challenges associated with fitting complex GLMM models, the bottom-up approach is more attractive in practice.

Bottom-Up GLMM Model Building

Step 1: Analyze a model with no predictor variables which includes random intercept effects.

Step 2: Analyze a model with all lower-level predictor variables treated as having 'fixed' effects. Assess the contribution of each variable to the model.

Step 3: Add the higher-level predictor variables to the model to see whether they explain between-group variation in the values of the response variable. Assess the contribution of each variable to the model.

Bottom-Up Model Building (cont'd)

Step 4: Assess whether any of the lower-level predictor variables has a significant slope variation across groups. Do this on a variable-by-variable basis.

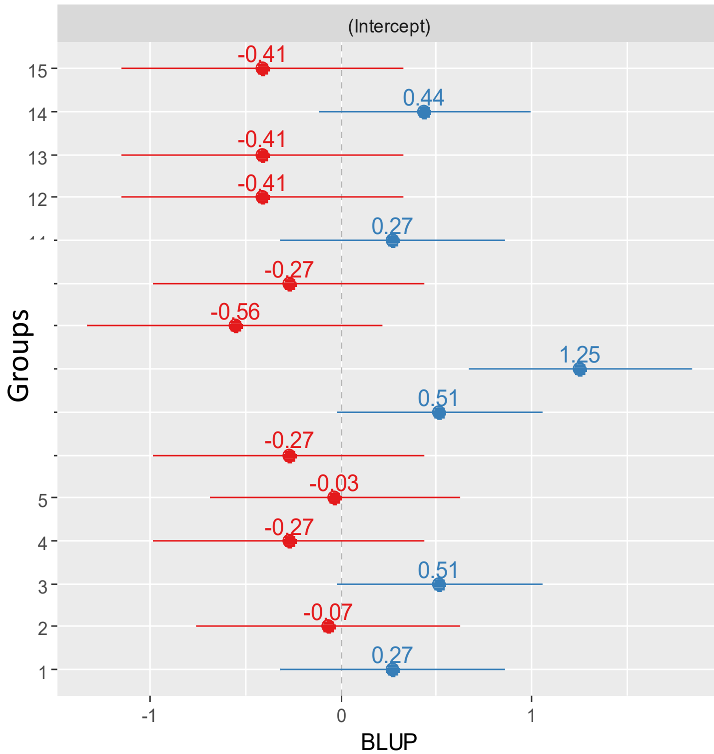
Step 5: Update the model in **Step 3** to simultaneously include all the relevant random effects for the lower level predictor variables.

Step 6: Add cross-level interactions between group level predictor variables and those individual-level predictor variables that had significant slope variation in **Step 4**.

Adapted from the book "Multilevel Analysis: Techniques and Applications," Second Edition, by Joop Hox (Routledge, 2010).

39

GLMM Diagnostics



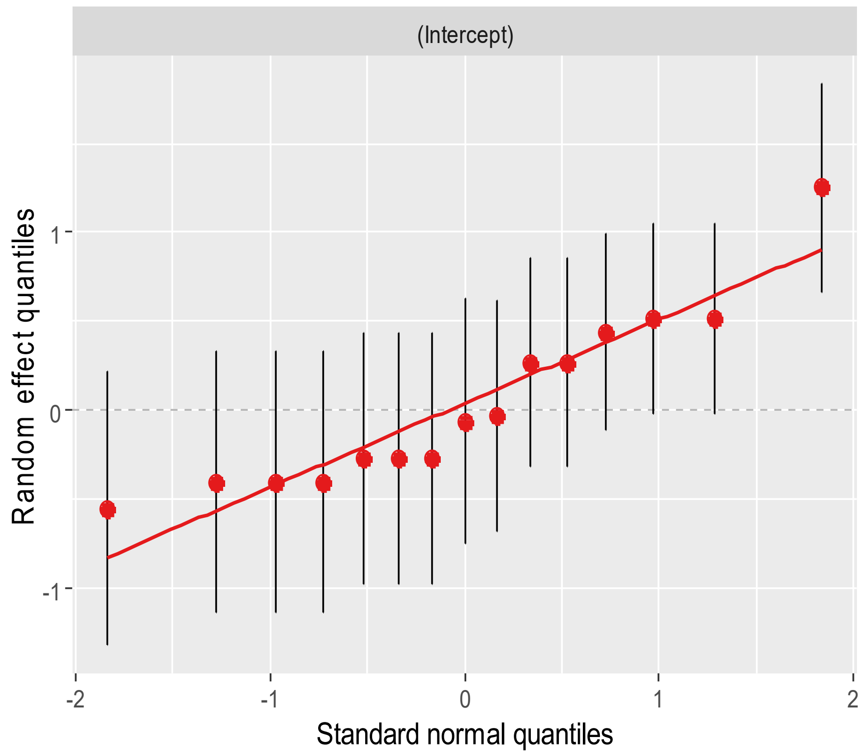
Random effects can be predicted (e.g., **B**est **L**inear **U**nbiased **P**rediction).

If there is interest in group behaviour, predicted random effects can be examined via forest plots in order to:

- ❑ Indicate how particular groups are doing;
- ❑ Rank or compare groups, or indicate unusual groups.

40

GLMM Diagnostics (cont'd)



Quantile-quantile plots can be used to assess the normality of the random effects.

If the normality assumption holds, the points in these plots should roughly line up along a straight line.

Summary

GLMMs can be difficult to understand, build, fit, and interpret.

However, they provide a flexible framework for analyzing non-normal response data with a ‘grouping’ structure.