# A Gentle Introduction to Generalized Linear Mixed Models – Part II

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THE ANALYSIS FACTOR





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# **G**eneralized **L**inear **M**ixed **M**odels (**GLMM**s)

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

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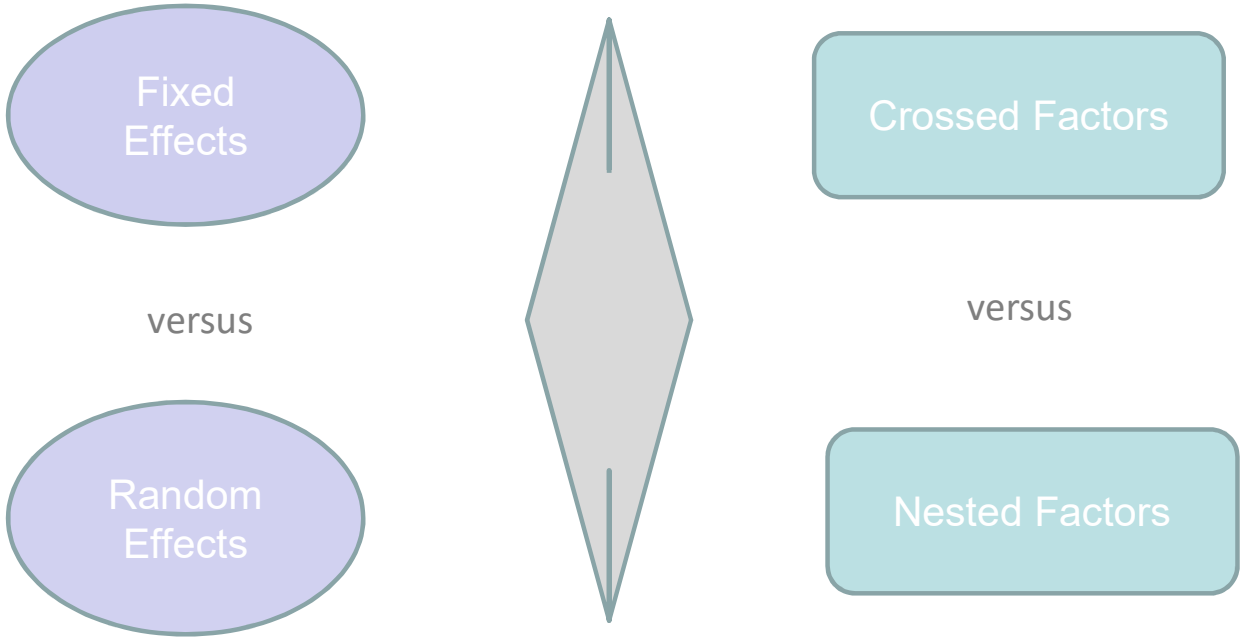
# Important Distinctions for GLMMs

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## Audience

Based on the first part of this webinar,
can you recall how fixed effects are different
from random effects in a GLMM?

What do you think happens if an effect should be modeled as random but is instead modeled as fixed?

What do you think happens if an effect should be modeled as fixed but is instead modeled as random?

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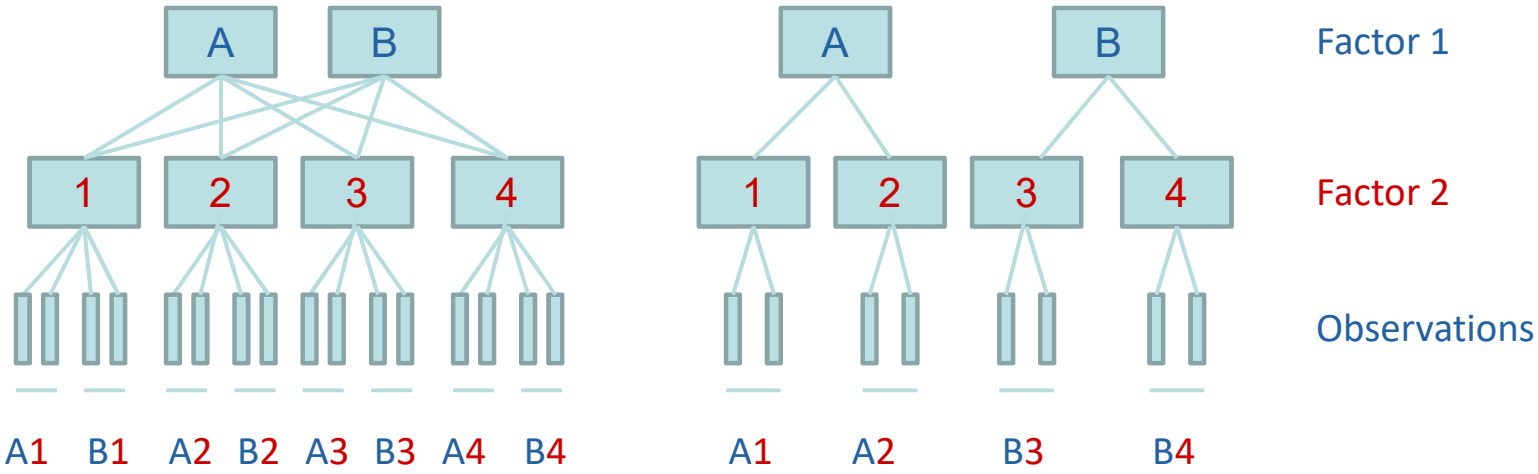
# Crossed versus Nested Grouping Factors




Factor 1 and Factor 2 are fully crossed

Factor 2 is nested in Factor 1

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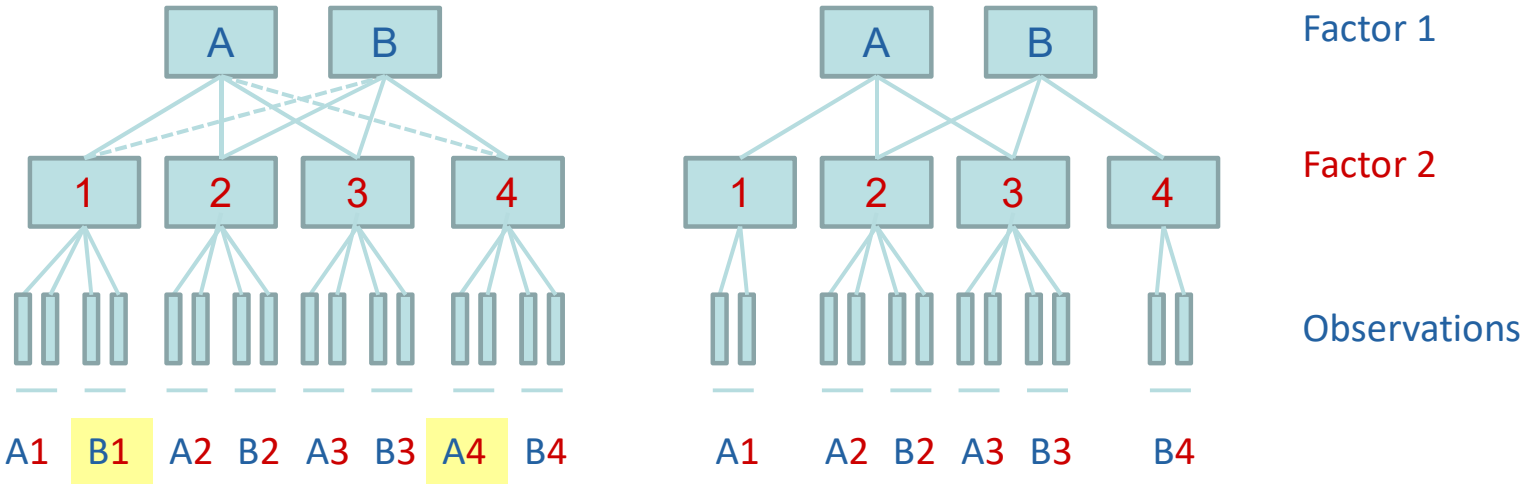
# Fully and Partially Crossed Grouping Factors




Factor 1 and Factor 2 are fully crossed

Factor 1 and Factor 2 are partially crossed

http://onlinelibrary.wiley.com/doi/10.1111/j.2041-210x.2012.00251.x/abstract

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## Audience

Can you give an example of a study with two random grouping factors such that the two factors are fully crossed?

Can you then modify your example so that the two grouping factors are nested?

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## Audience

Why do you think it is important to distinguish between crossed and nested grouping factors?

What do you think may happen if this distinction is not made?

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# Software Choices for Fitting GLMMs

| | | |
|---|---|---|
| **R**<br>lme4<br>MCMCglmm<br>MASS | **SAS**<br>GLIMMIX<br>NLMIXED | **STATA**<br>xtmixed<br>gllamm |
| **SPSS 19+**<br>GENLINMIXED | **MLWin** | **ASReml** |

http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0112653

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## Audience

What software are you currently using (or plan on using) to fit GLMMs?

Do you know what type of estimation method is used by that software for GLMMs?

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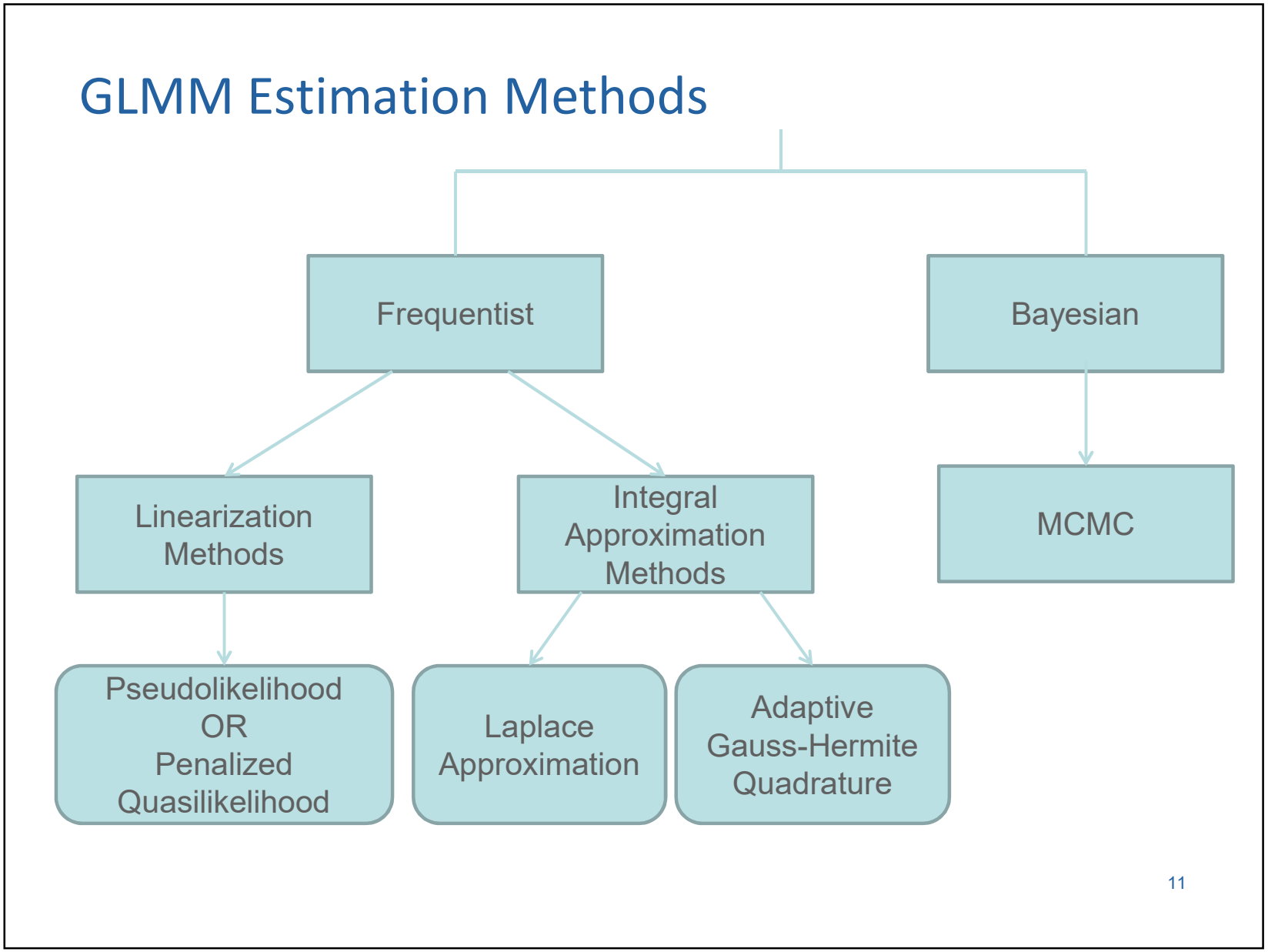

# Pros and Cons of Frequentist Estimation Methods

## Linearization Methods

- Estimate a pseudolikelihood instead of the true likelihood, raising questions about utility for inference
- May not yield usable estimates of the true likelihood
- Often give biased estimates when the random effect variances are large
- May not even yield parameter estimates in special cases (e.g., count data with lots of zeroes)

## Integral Approximation Methods

- Estimate the true likelihood, having an advantage for inference over Linearization Methods
- More accurate than Linearization Methods
- Slower than Linearization Methods
- Adaptive Gauss-Hermite Quadrature is more accurate than Laplace Approximation, but slower

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## Why Care About the GLMM Estimation Method?

For highly complex GLMM models (e.g., multiple grouping factors and/or many random effects), integral approximation methods may be computationally very intense and slow.

In this case, we may have no choice but to use faster estimation methods.

For example:

- ✓ Linearization Methods instead of Integral Approximation Methods
- ✓ Adaptive Gauss-Hermite Quadrature instead of Laplace Approximation

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# Why Care About the GLMM Estimation Method?

## Linearization Methods

- Likelihood ratio tests of significance of fixed effects are NOT available
- Only Wald tests of significance of fixed effects are reported
- Do not allow inferences concerning the variance of the random effects (Wald testing should NOT be used as it is grossly conservative!)

## Integral Approximation Methods

- Both likelihood ratio and Wald tests of significance of fixed effects are available
- Allow inferences concerning the variance of the random effects via likelihood ratio testing
- Allow computation of AIC
- Allow model selection via AIC

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# Audience: What type of GLMM estimation method was used to produce the output below?

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

 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
```

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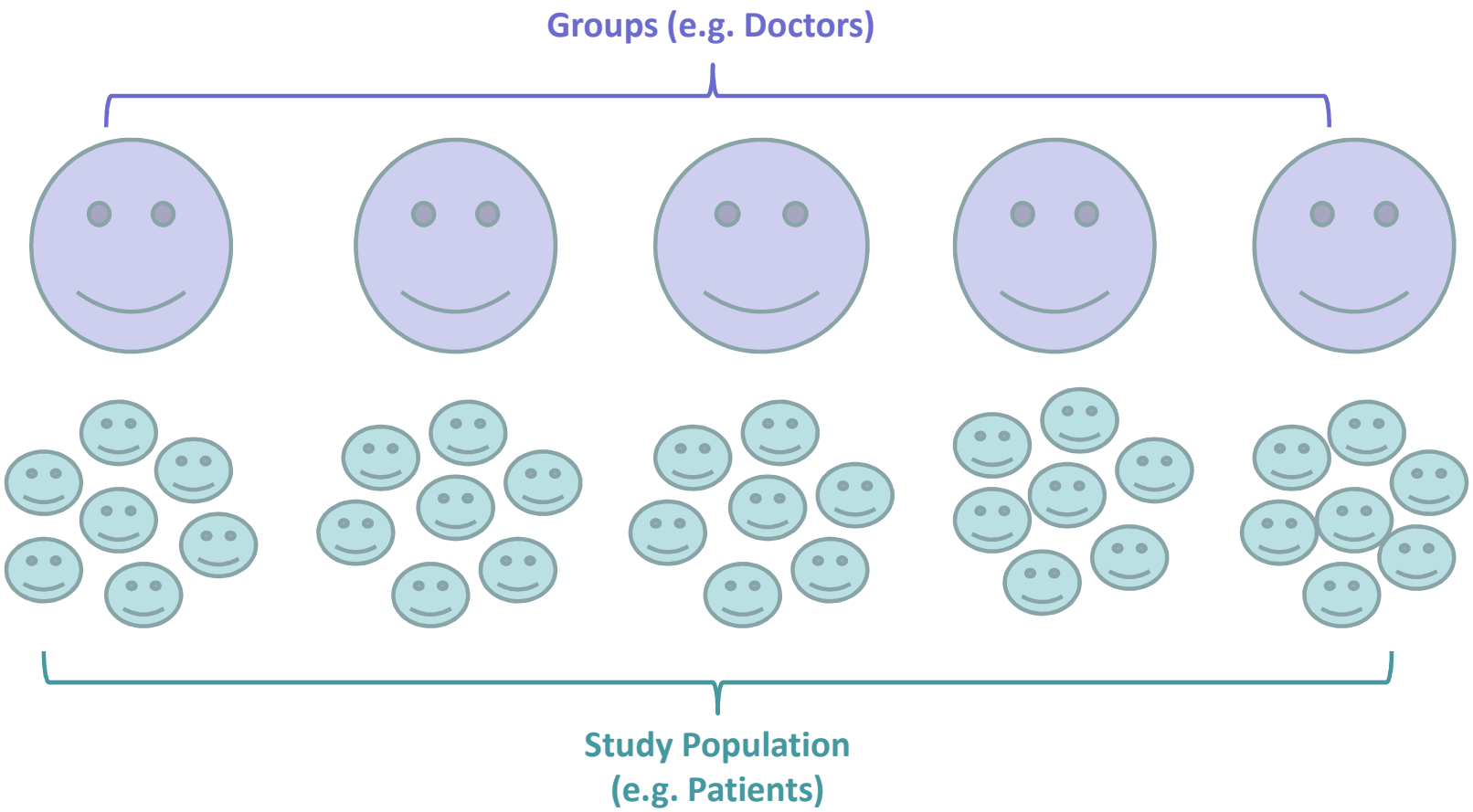
# Interpretation Pitfalls for GLMMs




GLMMs produce group-specific NOT population-averaged effects.

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# Interpretation Pitfalls for GLMMs

**Example No. 1**

**Outcome:** Tumor Development (yes vs. no)

**Predictor:** Age

GLMM looks at the doctor-specific effect of Age on Tumor Development.

The effect of Age represents a contrast between two patients who see the same doctor* (e.g., the "average" doctor) and whose ages are 1 year apart.

*Or different doctors with the same random effect value.

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# Interpretation Pitfalls for GLMMs

**Example No. 2**

**Outcome:** Number of Tumors

**Predictor:** Age

A GLMM looks at the effect of Age on Number of Tumors, conditional on doctor.

The effect of Age represents a contrast between two patients who see the same doctor* and whose ages are 1 year apart.

*Or different doctors with the same random effect value.

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# Interpretation Pitfalls for GLMMs

## In the previous examples, what does it mean to condition on the random effect of doctor when interpreting the Age effect?

It means to hold constant all of the doctor-specific influences on the outcome variable that are captured by the random doctor effect:

- Observed influences that were NOT included in the GLMM model;
- Unobserved influences.

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## Interpretation Pitfalls for GLMMs

In contrast, a marginal model such as the GEE model, would produce a population-averaged effect of Age.

That effect would be expressed as a contrast between two patients **in the study population** whose ages are 1 year apart.

The population-averaged effect of Age would therefore be obtained by 'averaging' across the doctor random effects.

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## Audience

Can you think of any other interpretation pitfalls for GLMMs?

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# Measures of Model Fit for GLMMs

**Marginal $R^2$**

**Conditional $R^2$**

Marginal $R^2$ is concerned with the proportion of outcome variability explained by the fixed factor(s) alone.

Conditional $R^2$ is concerned with the proportion of outcome variability explained by both fixed and random factors.

Difference between conditional and marginal $R^2$ reflects how much of the outcome variability is explained by the random factors.

Nakagawa, S., and H. Schielzeth. 2013. A general and simple method for obtaining $R^2$ from generalized linear mixed-effects models. Methods in Ecology and Evolution 4(2): 133-142. DOI: 10.1111/j.2041-210x.2012.00261.x

Johnson, Paul C.D. 2014. Extension of Nakagawa & Schielzeth's $R^2_{GLMM}$ to random slopes models. Methods in Ecology and Evolution. DOI: 10.1111/2041-210X.12225.

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## Audience

Someone reported the following GLMM results:

"The conditional R-squared for our GLMM model was found to be 0.9351 while the marginal R-squared was 0.9891."

What problem do you see with these results? Can you think of a reason why these results may not make sense?

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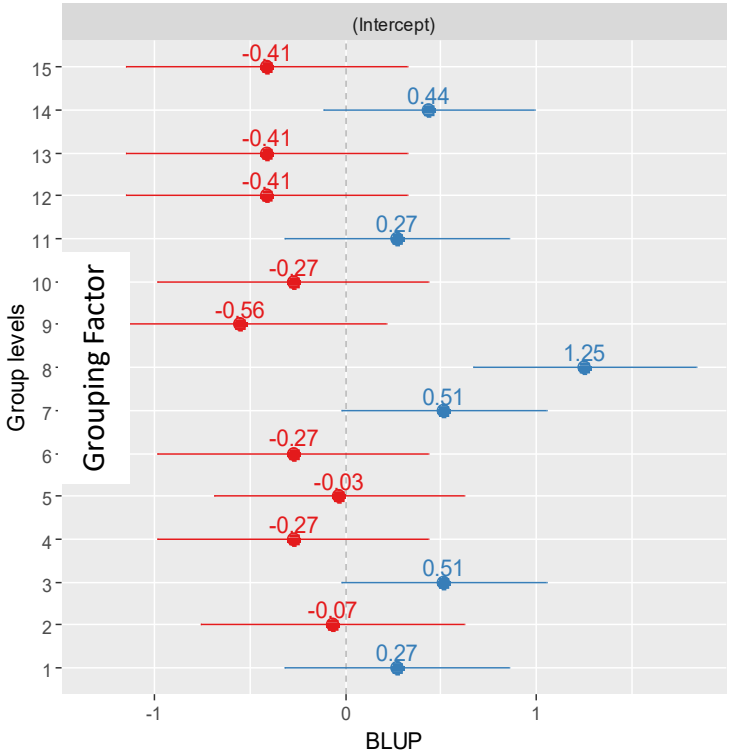
# GLMM Diagnostics




Random effects associated with a grouping factor or a lower-level predictor variable 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.

Annotated dots represent predicted random effects associated with the levels of a grouping factor which were included in the study.

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## Audience

- What do you think the vertical dotted line in the previous plot stands for?
- What about the horizontal lines? Why do you think some horizontal lines are wider than others?
- How would you re-arrange the previous plot to make it easier to rank groups?
- What would you look for in the previous plot in order to single out unusual groups?

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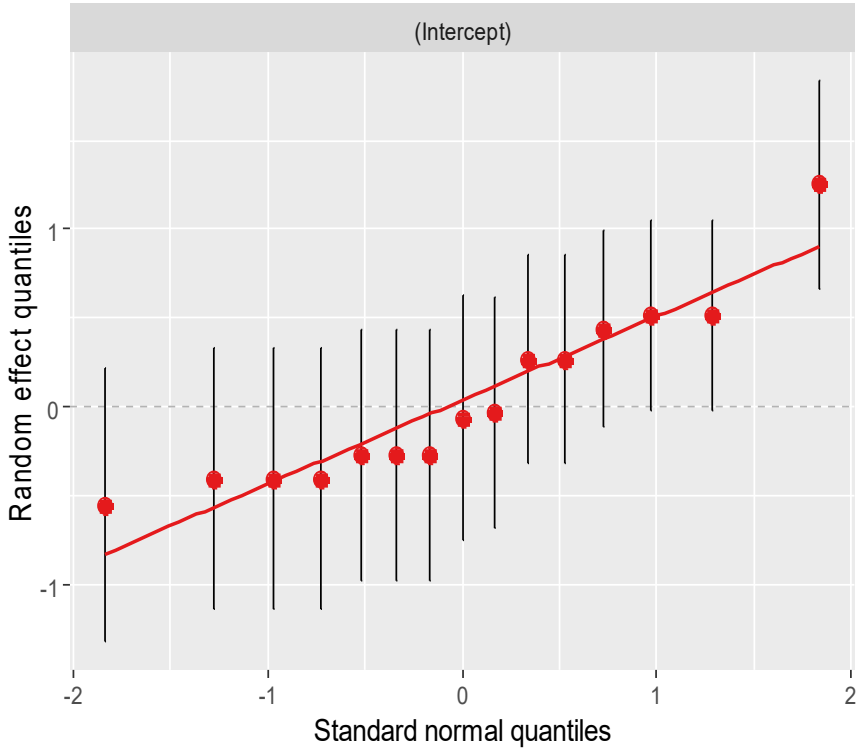
# GLMM Diagnostics




Quantile-quantile plots can be used to assess the normality of the random effects associated with a grouping factor or a lower-level predictor variable.

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

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## Audience

Does the quantile-quantile plot shown on the previous slide indicate any violations of the normality assumption?

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# Resources for Learning More about GLMMs

http://www.bristol.ac.uk/cmm/learning/online-course/index.html

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

http://ms.mcmaster.ca/~bolker/R/misc/foxchapter/bolker_chap.html

http://glmm.wikidot.com/

Bolker, B., Brooks, M., Clark, C., Geange, S., Poulsen, J., Stevens, M., & White, J. (2009). Generalized linear mixed models: a practical guide for ecology and evolution *Trends in Ecology & Evolution, 24* (3), 127-135 DOI: 10.1016/j.tree.2008.10.008

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# Summary

GLMMs require more computational and conceptual know-how to implement and interpret than linear mixed effects models.

But, once mastered, they open up the door to exciting applications which involve analyzing non-normal response data with a 'grouping' structure.

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