Interpretation of β in GEE and GLMM

Recall GEE:

$$g(\mu_{ij}) = \mathbf{X}_{ij}^T \beta$$

Recall GLMM:

$$g(\mu_{ij}^{\mathbf{b}}) = \mathbf{X}_{ij}^T \beta + \mathbf{Z}_{ij}^T \mathbf{b}_i$$

Question 2: Do they have the same interpretation?

Answer 2: Sometimes, but often not.

- For normal and count data (log-linear model with intercept), β has the same interpretation in GEEs and GLMMs.
- For binary data, β has different interpretations in GEEs and GLMMs.

Interpretation of β in GEE and GLMM (2)

Outside of special cases:

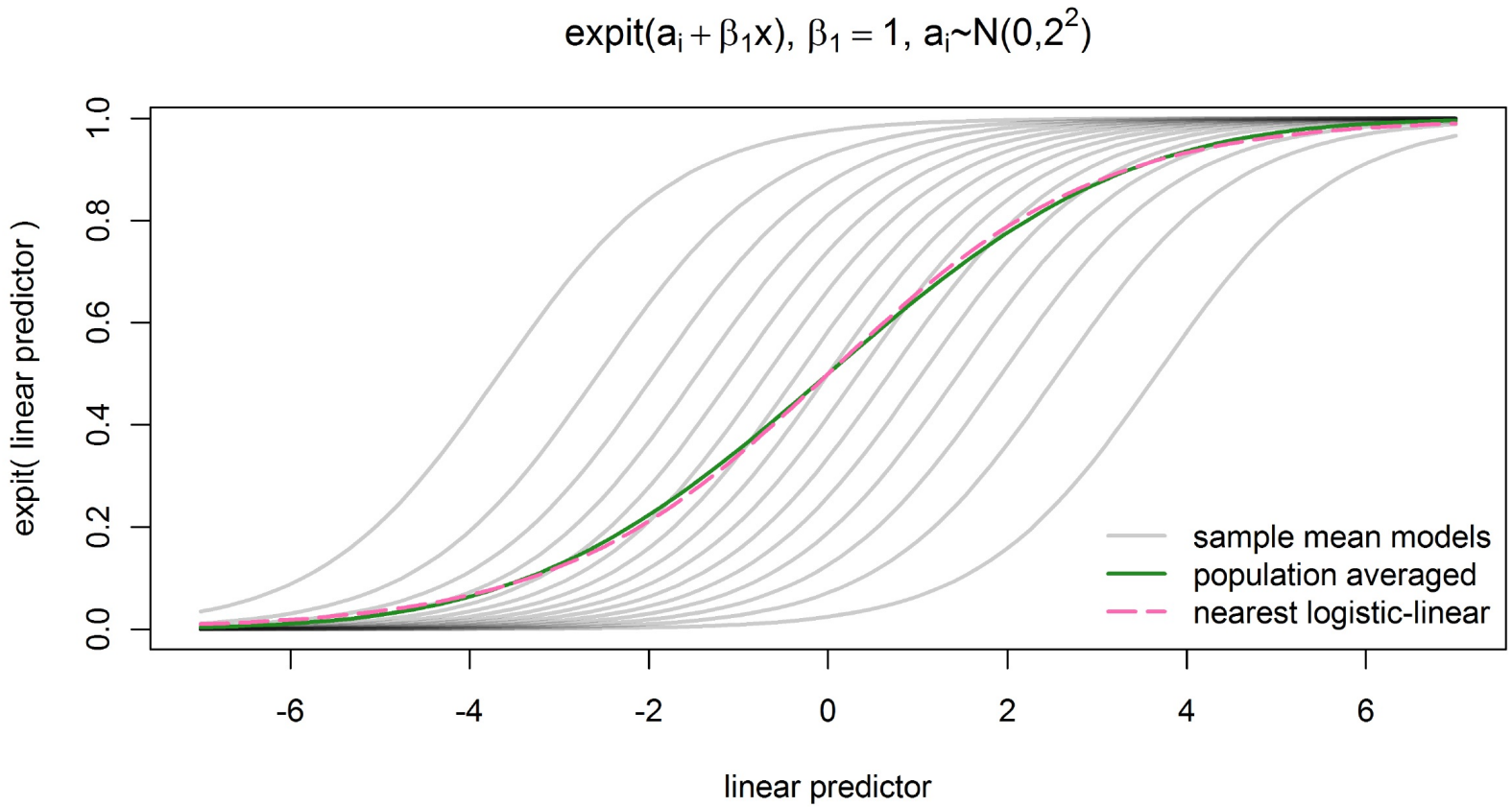
β in GEEs

- β has population-average interpretation
  - Average evolution of the outcome
- We are asking: *What is the log(OR) comparing the exposed population with the unexposed population?*

β in GLMMs

- β has subject specific interpretation
- The interpretation is conditional on the subject-specific random effects, $\mathbf{b}_i$
  - β models evolution of each individual subject separately
- We are asking: *What is the log(OR) if the same person were to change from unexposed to exposed?*

Logistic Example of Marginal vs. Conditional



Shamelessly borrowed from Adam

More on Differences in Interpretation (1)

Example: Neuhaus, Kalbfleish, and Hauck (1991):

- Study of whether a sample of breast fluid could $(Y = 1)$ or could not $(Y = 0)$ be obtained
- Covariates:

  X_1 = Dysplasia (breast specific)
  X_2 = Age
  X_3 = Age at menarche
  X_4 = Indicator for parous (given birth before)

More on Differences in Interpretation (2)

Example continued: Candidate Modelling Strategies:

- Logistic Mixed Model:

$$logitP(Y_{ij} = 1|\alpha_i, \mathbf{X}_{ij}) = \alpha_i + \beta \mathbf{X}_{ij}$$

β is change in conditional logit of the probability of response with covariate X for individuals in each of the underlying risk groups described by α_i

- Marginal Model:

$$logitP(Y_{ij} = 1|\mathbf{X}_{ij}) = \alpha^* + \beta^* \mathbf{X}_{ij}$$

β^* is change in logit of probability of response

More on Differences in Interpretation (3)

Example continued: Analysis results:

Point estimates (standard errors) of regression coefficients for cluster-specific and population-averaged approaches applied to data on the availability of breast fluid.

Variable	Mixed effects, β_{CS}	Liang–Zeger, β_{PA}	Ratio, β_{PA}/β_{CS}
Intercept	−1·951 (2·49)	−0·620 (0·908)	
Dysplasia	0·609 (0·462)	0·208 (0·155)	0·351
Age	0·146 (0·044)	0·050 (0·015)	0·343
Age at menarche	−0·414 (0·172)	−0·147 (0·059)	0·355
Full term birth	1·249 (0·610)	0·435 (0·216)	0·348
std. dev. (α_i)	4·218 (0·511)		

More on Differences in Interpretation (4)

Example continued: Discussion:

"Although the cluster-specific model seems to provide the more unified approach, parameter interpretation in these models is difficult. The cluster-specific model presupposes the existence of latent risk groups indexed by b_i, and parameter interpretation is with reference to these groups. No empirical verification of this statement can be available from the data unless the latent risk groups can be identified. Since each individual is assumed to have her own latent risk b_i, the model almost invites an unjustified causal statement about the change in odds of fluid availability for a given woman who ceases to be nulliparous."

More on Differences in Interpretation (5)

Example continued: Discussion:

"With covariates that vary within clusters, such as dysplasia, the mixed effect model provides a more satisfactory interpretation. The estimated coefficient for dysplasia, however, involves both a within cluster comparison based on differences between breasts for the same woman, and a between cluster comparison of average levels. An alternative and perhaps preferable analysis would partition dysplasia into average level of dysplasia for between cluster comparisions and departures from average for within cluster comparisons and allow separate coefficients for these two covariates. Population-averaged comparisons, on the other hand, make no specific use of within cluster comparisons for cluster varying covariates and substantially underestimate within cluster risks."

More on Differences in Interpretation (6)

Example continued: More Discussion:

- "In population-averaged models, the effects are based on averaging over subpopulations defined in the specific covariates in the model. As one adds covariates the attenuation... will be reduced; the averaging is done over ever-smaller groups with a particular risk group and the corresponding cluster-specific measure of effect as the limit."

- "Cluster-specific models are best equipped to address questions relating to modification of a particular cluster (and hence must be used with caution unless the variable of is cluster varying and experimentally manipulated) since population-averaged models not estimate this effect"

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More on Differences in Interpretation (6)

Example continued: More Discussion:

- "The odds ratios cluster-specific and population-averaged models, although quite different in magnitude, are in fact describing exactly the same dependence of risk on the covariates. Neither truly be interpreted or understood without reference to the baseline risk."
- "In the population-averaged case, the baseline risk is simply the proportion of positive responses at the standard level of the covariate"
- "in the cluster-specific case, the baseline risk is in fact a distribution of risks"
- "With this convention, the two analyses provide the same qualitative assessment"