BIOS 755: Linear Mixed Models I

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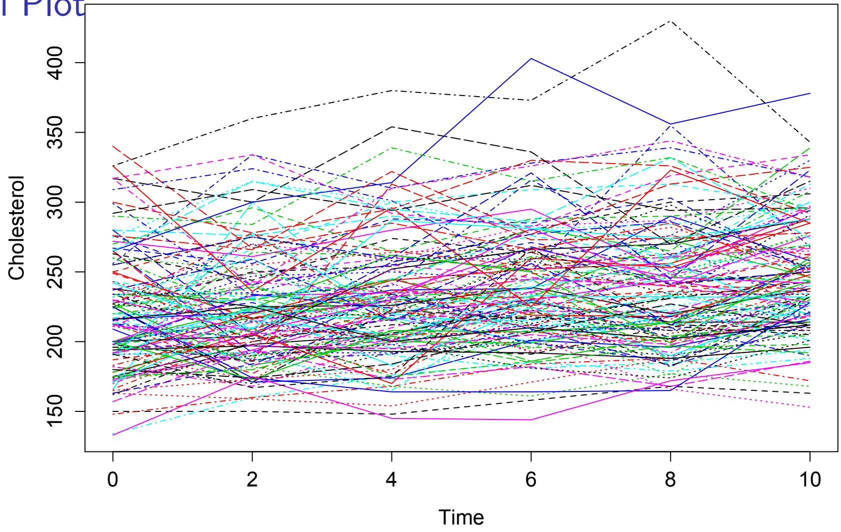
Framingham study Cholesterol Data

- In the Framingham study, each of 2634 participants was examined every 2 years for a 10 year period for his/her cholesterol level.
- Study objectives:
  - How does cholesterol level change over time on average as people get older?
  - How is the change of cholesterol level associated with sex and baseline age?
- A subset of 200 subjects' data is used for illustrative purpose.

Spaghetti Plot



Introduction to Linear Mixed Models

- In the General Linear Model we focused our conceptual model on the covariance and correlation of the error terms.
- In linear mixed models, the conceptual model is based on thinking about individual behavior first.
- The possibilities for how this is represented and how the variation in the population is represented, are very flexible.
- As we'll see, linear mixed models can incorporate heterogeneity and different correlation structures (even though we don't think about them that way).

Linear Mixed (Effects) Models

- The linear mixed model can be expressed as

$$\boldsymbol{Y}_i = \boldsymbol{X}_i\boldsymbol{\beta} + \boldsymbol{Z}_i\boldsymbol{b}_i + \boldsymbol{e}_i$$

where

- $\boldsymbol{X}_i$ – $n_i \times p$ matrix of fixed effect covariates
- $\boldsymbol{\beta}$ – $k \times 1$ vector of regression coefficients (fixed effects).
- $\boldsymbol{Z}_i$ – $n_i \times q$ matrix of random effect covariates.
- $\boldsymbol{b}_i$ – $q \times 1$ vector of random effects, $\boldsymbol{b}_i \sim N(0, \boldsymbol{G})$,
- $\boldsymbol{e}_i$ – $n_i \times 1$ vector of errors and $\boldsymbol{e}_i \sim N(0, \boldsymbol{R}_i)$.

Random intercept and slope model

The random intercept and slope model:

$$\boldsymbol{Y}_i = \beta_0 + b_{0i} + (\beta_1 + b_{1i})\boldsymbol{t}_i + \boldsymbol{e}_i$$

where $\boldsymbol{t}_i' = \{t_{i1}, t_{i2}, \ldots, t_{in_i}\}$

- β_0 is the average intercept and b_{0i} are the deviations from the average intercept.
- β_1 is the average slope and b_{1i} are the deviations from the average slope.
- We could add other fixed effects to this model (sex, smoking, etc.).

Random intercept and slope model

The random intercept and slope model:

$$\boldsymbol{Y}_i = \beta_0 + b_{0i} + (\beta_1 + b_{1i})\boldsymbol{t}_i + \boldsymbol{e}_i$$

- $\boldsymbol{R}_i = var(\boldsymbol{e}_i)$ describes the covariance of the residuals
- In the models we've been running in the previous weeks, this is the covariance of the ith subject's deviations from $\beta_0 + \beta_1 \boldsymbol{t}_i$ (i.e., the overall trend)
- Now it's the covariance of the ith subject's deviations from $\beta_0 + b_{0i} + (\beta_1 + b_{1i})\boldsymbol{t}_i$ (i.e., their individual trend)
  - Usually, it is assumed that $\boldsymbol{R}_i = \sigma^2 I$, which is the "conditional independence assumption."

Linear Mixed (Effects) Models

$$\boldsymbol{Y}_i = \boldsymbol{X}_i\boldsymbol{\beta} + \boldsymbol{Z}_i\boldsymbol{b}_i + \boldsymbol{e}_i$$

The vector of regression parameters $\boldsymbol{\beta}$ are the fixed effects, which are assumed to be the same for all individuals.

- Fixed effects are constant across individuals, and random effects vary.
- For example, in a growth study, a model with random intercepts $\beta_0 + b_{0i}$ and fixed slope β_1 corresponds to parallel lines for different individuals i, or the model $Y_{ij} = \beta_0 + b_{0i} + \beta_1 t_{ij} + e_{ij}$

Conditional vs marginal mean

- The **conditional** mean of $\boldsymbol{Y}_i$, given $\boldsymbol{b}_i$, is

$$E(\boldsymbol{Y}_i|\boldsymbol{b}_i) = \boldsymbol{X}_i\beta + \boldsymbol{Z}_i\boldsymbol{b}_i$$

- The **marginal** or **population-averaged** mean of $\boldsymbol{Y}_i$ is

$$E(\boldsymbol{Y}_i) = \boldsymbol{X}_i\beta$$

- In contrast to β, the vector $\boldsymbol{b}_i$ is comprised of subject-specific regression coefficients.
- All covariates in $\boldsymbol{Z}$ will be in $\boldsymbol{X}$, and it's rare to consider more than 2 variables in $\boldsymbol{Z}$.

Conditional vs marginal variance

- In the mixed model

$$\boldsymbol{Y}_i = \boldsymbol{X}_i\beta + \boldsymbol{Z}_i\boldsymbol{b}_i + \boldsymbol{e}_i$$

- We have the following conditional and marginal expectations

$$E(\boldsymbol{Y}_i|\boldsymbol{b}_i) = \boldsymbol{X}_i\beta + \boldsymbol{Z}_i\boldsymbol{b}_i, \quad E(\boldsymbol{Y}_i) = \boldsymbol{X}_i\beta$$

  along with the following conditional and marginal variances

$$\begin{aligned} var(\boldsymbol{Y}_i|\boldsymbol{b}_i) &= var(\boldsymbol{e}_i) = \boldsymbol{R}_i, \quad \text{and} \\ var(\boldsymbol{Y}_i) &= var(\boldsymbol{Z}_i\boldsymbol{b}_i) + var(\boldsymbol{e}_i) \\ &= \boldsymbol{Z}_i\boldsymbol{G}\boldsymbol{Z}_i' + \boldsymbol{R}_i \end{aligned}$$

Linear Mixed (Effects) Models

- The introduction of random effects induces correlation among the $\boldsymbol{Y}_i$.
- $Var(\boldsymbol{Y}_i)$ is described in terms of a set of covariance parameters, some defining $\boldsymbol{G}$ and some defining $\boldsymbol{R}_i$.
- Linear mixed models are really just another type of covariance matrix, which can lead to some strange results.
- They are the model of choice when the data are unbalanced.