A general LMM has the following form:

$$y_{it_{ij}} = \mathbf{x}_{it_{ij}}^\top \boldsymbol{\beta} + \mathbf{z}_{it_{ij}}^\top \mathbf{b}_i + \epsilon_{it_{ij}}, \quad \mathbf{y}_i = X_i \boldsymbol{\beta} + Z_i \mathbf{b}_i + \boldsymbol{\epsilon}_i, \quad \mathbf{b}_i \perp \boldsymbol{\epsilon}_i \qquad (4.10)$$
$$\mathbf{b}_i \sim \text{i.i.d.} N(0, D), \quad \boldsymbol{\epsilon}_i \sim \text{i.i.d.} N\left(0, \sigma^2 \mathbf{I}_{m_i}\right), \quad 1 \le j \le m_i$$

where $\mathbf{x}_{it}^\top \boldsymbol{\beta}$ is the fixed and $\mathbf{z}_{it}^\top \mathbf{b}_i$ the random effect, $\perp$ denotes stochastic independence and $W_i = \left(\mathbf{w}_{it_{i1}}, \ldots, \mathbf{w}_{it_{im_i}}\right)^\top$ ($W = X$ or Z). For growth-curve analysis (modeling change of y_{it} over time as in longitudinal study), $\mathbf{z}_{it}$ is often equal to $\mathbf{x}_{it}$. It follows from the assumptions of the LMM that:

$$E(\mathbf{y}_i \mid X_i, Z_i) = X_i \boldsymbol{\beta}, \quad Var(\mathbf{y}_i \mid X_i, Z_i) = Z_i D Z_i^\top + \sigma^2 \mathbf{I}_{m_i} \qquad (4.11)$$

Clustered data also often arise from cross-sectional studies. For example, psychotherapy or behavioral intervention programs in the behavioral and social sciences are often delivered in a group format. Because therapists may differ in their skill set or ability to form a therapeutic bond and alliance with their patients, which are important considerations for intervention effect, there are often real differences between therapists. Such variability leads to different treatment outcomes in patients who are treated by different therapists and should be accounted for in assessing treatment effect in such studies.

Example 6 (*LMM for controlling for therapists' effect*). Let n denote the number of therapists and m_i the number of patients seen by the ith therapist in a cross-sectional study comparing two treatment conditions ($1 \le i \le n$). By treating n as the number of clusters and m_i as the size of each cluster, patient's response, y_{ij}, can be modeled using the following LMM:

$$y_{ij} = \beta_0 + x_i \beta_1 + b_i + \epsilon_{ij}, \quad b_i \sim \text{i.i.d.} N\left(0, \sigma_b^2\right) \qquad (4.12)$$
$$\epsilon_{ij} \sim \text{i.i.d.} N\left(0, \sigma^2\right), \quad 1 \le i \le n, \quad 1 \le j \le m_i$$

where the binary x_i indicates the treatment conditions. In the above, b_i accounts for the individual effect of the ith therapist with σ_b^2 measuring the variability across therapists. Thus, concerns about therapists' variability can be examined by testing the null hypothesis: $H_0 : \sigma_b^2 = 0$. Note that in this example, $\mathbf{x}_{it} = (1, x_i)^\top \neq \mathbf{z}_{it} = 1$.

Example 7. For the LMM in (4.12) of Example 6, we have:

$$Var(\mathbf{y}_i \mid x_i) = \left(\sigma_b^2 + \sigma^2\right) C_{m_i} \left(\frac{\sigma_b^2}{\sigma_b^2 + \sigma^2}\right) \qquad (4.13)$$