## Simulating the unobserved and the slope conditional on the observed

Let Y denote the observed lipid and U denote the unobserved. Our model for  $U_{it}$ , the unobserved 'true' lipid at time t, in a person i, is

$$U_{it} = \alpha_i + t\beta_i + A_i\gamma$$

where  $A_i$  is the age of person *i* at time 0,  $\alpha_i \sim N(\alpha, \sigma_a^2)$  and  $\beta_i \sim N(\beta, \sigma_b^2)$ with  $\text{Cov}(\alpha_i, \beta_i) = \sigma_{ab}$ . Our models for the observed, conditional on the unobserved, is

$$Y_{it} \sim N\left(U_{it}, \sigma_w^2\right)$$

Then

$$\begin{pmatrix} \beta_i \\ \alpha_i \\ Y_{i0} \end{pmatrix} | A_i \sim N \left( \begin{pmatrix} \beta \\ \alpha \\ \alpha + \gamma A_i \end{pmatrix}, \begin{pmatrix} \sigma_b^2 & \sigma_{ab} & \sigma_{ab} \\ \sigma_{ab} & \sigma_a^2 & \sigma_a^2 \\ \sigma_{ab} & \sigma_a^2 & \sigma_a^2 + \sigma_w^2 \end{pmatrix} \right)$$

Then, given  $Y_{i0}$  and  $A_i$ , the distribution of  $\alpha_i$  is

$$\alpha_i | Y_{i0}, A_i \sim N\left(\alpha + \frac{\sigma_a^2}{\sigma_a^2 + \sigma_w^2} \left(Y_{i0} - \alpha - \gamma A_i\right), \sigma_a^2\left(1 - \frac{\sigma_a^2}{\sigma_a^2 + \sigma_w^2}\right)\right)$$

The only thing in this expression that varies by patient is  $Y_{i0}$ , so a person-specific mean can be calculated, then  $\alpha_i$  can be simulated from a Normal distribution.

Having given every patient a simulated  $\alpha_i$ , their  $\beta_i$  can be simulated conditional on  $\alpha_i$ .

$$\beta_i | \alpha_i \sim N\left(\beta + \frac{\sigma_{ab}}{\sigma_a^2} \left(\alpha_i - \alpha\right), \sigma_b^2 - \frac{\sigma_{ab}^2}{\sigma_a^2}\right)$$

Notice that in the final term of the variance, the numerator is  $\sigma_{ab}^2$  not  $\sigma_{ab}$ .

## Note on derivation

These calculations are based on this result from standard properties of the multivariate normal distribution. If

$$\begin{pmatrix} X_1 \\ X_2 \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix}, \begin{pmatrix} \Sigma_{11} & \Sigma_{12} \\ \Sigma_{21} & \Sigma_{22} \end{pmatrix}\right)$$

Then  $X_1$  conditional on  $X_2 = x_2$  has Normal distribution with mean

$$\mu_1 + \Sigma_{12} \Sigma_{22}^{-1} \left( x_2 - \mu_2 \right)$$

and variance

$$\Sigma_{11} - \Sigma_{12} \Sigma_{22}^{-1} \Sigma_{21}$$

Source:

http://www.public.iastate.edu/~vardeman/stat447/mvnfacts.pdf