9

Fixed Effects versus Random Effects Models

9.1 INTRODUCTION

In the previous chapter we discussed linear mixed effects models for longitudinal data. The key feature of the models was the introduction of random effects to account for natural heterogeneity in the study population. An alternative, but closely related, class of linear regression models for longitudinal data have their origins in the econometrics literature where they are known as "fixed effects" models. These so-called fixed effects models are increasingly used in the social sciences, broadly defined, and differ in a number of important ways from the mixed effects models considered in Chapter 8. In this chapter, we review the main features of linear fixed effects models for longitudinal data and discuss their potential advantages and disadvantages relative to linear mixed effects models. We highlight the key differences between the two modeling approaches using a numerical illustration. We also apply both modeling approaches to lung function growth data from the Six Cities Study of Air Pollution and Health. Finally, we discuss a mixed effects model for longitudinal data that incorporates the most desirable features of both classes of models via an appropriate decomposition of between- and within-subject effects.

9.2 LINEAR FIXED EFFECTS MODELS

Recall that one important motivation for the use of regression models is the control of confounding. In longitudinal studies where randomization cannot be employed, great emphasis must be placed on the measurement and control of important confounding

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variables. By construction, regression models allow the assessment of the effects of the covariates of main scientific interest while statistically adjusting or controlling for confounding variables that have also been included in the analysis. Of course, this type of adjustment for confounding has at least two limitations. First, no matter how many confounding variables have been incorporated into the regression model, the resulting analysis is always open to the critique that some critical confounders have been omitted. Second, even if it were possible to have complete consensus on the full list of potential confounders, it is almost certain that some of these variables would be inherently difficult or prohibitively expensive to measure. As a result it is almost inevitable that most non-randomized studies will fail to measure all of the key potential confounders and the results of any regression analysis must be interpreted with some caution. Fixed effects models were developed with the goal of overcoming both of these limitations, at least for one particular type of confounding variable in a longitudinal study.

Linear fixed effects models were introduced by econometricians with the intended goal of eliminating an important potential source of bias from regression models for longitudinal data. The fundamental idea underlying fixed effects models is the control of all potential confounding variables that remain stable across repeated measurement occasions and whose effects on the response are assumed to be constant over time. That is, fixed effects models were developed with the goal of removing the potential confounding effects of both observed and unobserved *time-invariant* confounders from longitudinal analyses, under the assumption that the effects of these confounders on the response remain constant over time. For their application to longitudinal data, fixed effects models require two features of the data: (1) two or more repeated measures of the response variable, and (2) values of the covariates of main interest must vary over measurement occasions, for at least some subset of the sample. The first requirement is trivial and is met, by definition, in all longitudinal studies. The second requirement implies that fixed effects models will be most useful in those settings where the main covariates of scientific interest are time-varying. Conversely, fixed effects models are not useful when it is also of interest to estimate the effects of time-invariant covariates.

Next we consider the statistical formulation of the linear fixed effects model. The notation we use is very similar to that employed in Chapter 8. To accommodate unbalanced data, we assume that there are n_i repeated measurements of the response on the i^{th} subject and that each Y_{ij} is observed at time t_{ij}. Associated with each response, Y_{ij}, there is a $p \times 1$ vector of covariates. The vector of covariates can be partitioned into two main types of covariates: covariates whose values do not change throughout the duration of the study and covariates whose values change over time. The former are referred to as time-invariant or between-subject covariates (e.g., gender and fixed experimental treatments), while the latter are referred to as time-varying or within-subject covariates (e.g., time since baseline, current smoking status, and environmental exposures). In a slight departure from the notation used in previous chapters, we let X_{ij} denote the $q \times 1$ vector of time-varying covariates and W_{ij} denote the $(p - q) \times 1$ vector of time-invariant covariates. For the latter, the same values of the covariates are replicated in the corresponding rows of W_{ij}, for $j = 1, ..., n_i$; so we can drop the second subscript and denote the time-invariant covariates by W_i. The linear fixed effects model is given by

$$Y_{ij} = X'_{ij}\beta + W'_i\gamma + \alpha_i + \epsilon_{ij}, \tag{9.1}$$

where the α_i are *fixed effects* representing stable (i.e., time-invariant) characteristics of individuals that are not otherwise accounted for by the inclusion of the time-invariant covariates, W_i, in the model. The model is completed by assuming the random within-subject errors, $\epsilon_{ij} \sim N(0, \sigma^2_\epsilon)$. At first glance, this model bears remarkable resemblance to the linear mixed effects model considered in Chapter 8, specifically, the random intercepts model. One of the key distinctions, however, is that in the fixed effects model formulation the α_i are considered to be fixed effects, whereas in the linear mixed effects model formulation the α_i are considered to be random. Unfortunately, there are many conflicting definitions of the terms "fixed effects" and "random effects" in the statistical literature and the use of this nomenclature leads to much confusion among statisticians and practitioners alike. As we will see, the key distinction between *fixed effects* models and *random effects* models is whether the α_i in (9.1) are assumed to be correlated with the covariates. Later we discuss the similarities and differences between these two classes of models in much greater detail.

We want to compare and contrast the fixed and mixed effects models in terms of their model assumptions. The fixed effects model makes the following assumptions about the relationships between X_{ij}, W_i, α_i, and ϵ_{ij}. First, X_{ij} is assumed to be completely independent of the random errors, not only ϵ_{ij} but also $\epsilon_{ij'}$ for $j' \neq j$. Importantly, this assumption implies that the current value of the response variable, Y_{ij}, given X_{ij}, does not predict the subsequent value of $X_{i,j+1}$. Econometricians refer to this as the assumption that X_{ij} is *strictly exogenous*. Some of the implications of the assumption of strict exogeneity are discussed in Chapter 13, Section 13.5. Second, the fixed effects model allows the α_i to be correlated with X_{ij}. It is the latter assumption that sets the fixed effects model apart from the mixed effects model considered in Chapter 8. That is, in the linear mixed effects model we assume that X_{ij} is *strictly exogenous* but make the additional assumption that the α_i, now considered random rather than fixed effects (and denoted by b_i in Chapter 8), are independent of X_{ij} (and independent of W_i, and ϵ_{ij}). Thus the mixed effects model, unlike the fixed effects model, requires the additional assumption that the random subject effects are uncorrelated with X_{ij} at all occasions $j = 1, ..., n_i$. Later we will discuss the implications of these assumptions for inferences about β (and γ).

At this point it is instructive to examine some features of the fixed effects model in the simplest possible longitudinal design with only two repeated measures. Also for simplicity, we assume that X_{ij} and W_i are both scalar, each comprised of a single time-varying and time-invariant covariate respectively. The fixed effects model is given by

$$Y_{ij} = \beta X_{ij} + \gamma W_i + \alpha_i + \epsilon_{ij}, \text{ for } j = 1, 2$$

(for simplicity, a model with intercept equal to zero is assumed). Under the assumptions of the fixed effects model, $\epsilon_{ij} \sim N(0, \sigma^2_\epsilon)$. It is tempting to try to estimate β,

γ, and the α_i via ordinary least squares (OLS) regression. However, any attempt to jointly estimate all of these effects will run afoul of the following difficulty: the α_i are perfectly collinear with γW_i. Consequently we cannot estimate both α_i and γ from the data at hand. Thus a very notable feature of fixed effects models is that they provide estimates only of the regression parameters for time-varying covariates. The effects of time-invariant covariates simply cannot be estimated in the fixed effects model formulation because of their perfect collinearity with α_i.

To estimate β, we can consider the model for the within-subject changes in the response, $Y_{i2} - Y_{i1}$,

$$\begin{aligned} Y_{i2} - Y_{i1} &= \beta X_{i2} + \gamma W_i + \alpha_i + \epsilon_{i2} - (\beta X_{i1} + \gamma W_i + \alpha_i + \epsilon_{i1}) \\ &= \beta(X_{i2} - X_{i1}) + (\epsilon_{i2} - \epsilon_{i1}). \end{aligned}$$

The regression model for the within-subject changes meets all of the usual assumptions of standard linear regression. Thus β can be estimated from the OLS regression of $(Y_{i2} - Y_{i1})$ on $(X_{i2} - X_{i1})$, using any standard linear regression software, because the error terms, $\epsilon_{i2} - \epsilon_{i1}$, have mean zero, $E(\epsilon_{i2} - \epsilon_{i1}) = 0$, and constant variance, $\text{Var}(\epsilon_{i2} - \epsilon_{i1}) = 2\sigma_\epsilon^2$. Note that in the construction of a model for the within-subject changes, both the time-invariant covariate effect and the stable (or time-invariant) characteristics of an individual, denoted by α_i, have disappeared from the model. This makes it clear that the α_i cannot possibly have any effect on the estimation of β, regardless of whether or not they are correlated with X_{ij}. Therefore, if the α_i are thought of as all those unmeasured, but time-invariant, characteristics of an individual, then the so-called fixed effects estimate of the effect of X_{ij} on Y_{ij} is unbiased even if some of those characteristics are considered to be confounders of the relationship between X_{ij} and Y_{ij}. It is in that sense that it can be said that the fixed effects model removes the potential for bias due to confounding by all measured and unmeasured time-invariant characteristics of individuals (the latter are encapsulated in the α_i). However, there is one important additional assumption that must not be overlooked. The fixed effects model can only remove the potential confounding by those measured and unmeasured time-invariant covariates *whose effects on the response remain constant over time*. That is, conditional on X_{ij} and W_i, it must be assumed that the effect of any time-invariant confounder on Y_{i1} is the same as on Y_{i2}.

Although in the illustration above we considered only two repeated measures, the same logic and rationale concerning properties of the fixed effects model apply more generally to the case of more than two repeated measures. In the more general case it can be shown that the fixed effects model estimator of β is the standard OLS estimator for "mean-centered" transformations[1] of Y_{ij} and the covariates. Here mean-centering simply involves taking averages over repeated measurement occasions separately for each individual and then transforming the response and covariates by subtraction of the subject-specific means for the response and covariates. Specifically, let $Y_{ij}^* =$

[1]In the econometrics literature, this mean-centered transformation is often referred to as a "demeaning" transformation; we avoid the use of this term lest we create the impression there is something improper about the subtraction of a mean.

$Y_{ij} - \overline{Y}_i$, where $\overline{Y}_i = \frac{1}{n_i}\sum_{j=1}^{n_i} Y_{ij}$, denote the mean-centered response for the i^{th} individual at the j^{th} occasion. In a similar fashion we can define the mean-centered covariates, $X^*_{ijk} = X_{ijk} - \overline{X}_{ik}$, where $\overline{X}_{ik} = \frac{1}{n_i}\sum_{j=1}^{n_i} X_{ijk}$. Note that mean-centering of W_i, the time-invariant covariates, removes all of the variation in these covariates so that $W^*_i = 0$ for all individuals. Because estimation in the fixed effects model is based entirely on within-subject variation in the response and covariates, it is now apparent why the effects of time-invariant covariates cannot be estimated; mean-centering of W_i sets $W^*_i = 0$ for all subjects and thereby removes all of the variation in these covariates. In a similar way, mean-centering makes the α_i disappear from the model.[2] It can be shown that the fixed effects estimator of β is simply the OLS estimator of the regression of the mean-centered response on the mean-centered covariates,

$$Y^*_{ij} = X^{*\prime}_{ij}\beta + \epsilon^*_{ij},$$

where $\epsilon^*_{ij} = \epsilon_{ij} - \overline{\epsilon}_i$. Interestingly, although the errors ϵ^*_{ij} in the mean-centered model are no longer uncorrelated over time for a given individual, the correlation among these errors can be ignored for estimation of β; that is, for the mean-centered model, the generalized least squares (GLS) estimator of β that accounts for the correlation among the ϵ^*_{ij} happens to be identical to the OLS estimator of β. The resulting fixed effects estimator of β, denoted $\widehat{\beta}^{(FE)}$, is

$$\widehat{\beta}^{(FE)} = \left(\sum_{i=1}^{N}\sum_{j=1}^{n} X^*_{ij}X^{*\prime}_{ij}\right)^{-1}\left(\sum_{i=1}^{N}\sum_{j=1}^{n} X^*_{ij}Y^*_{ij}\right).$$

An important property of this estimator is that it is unbiased for β, even in cases where the α_i are correlated with X_{ij}.

To summarize, the main appeal of fixed effects models is their statistical control of time-invariant characteristics of individuals whose effects on the response are assumed to remain constant over time. An important feature of these models is that they have the potential to remove bias when there are unmeasured, but stable, characteristics of the subjects that are correlated with time-varying covariates of main scientific interest. Of note, fixed effects models cannot estimate the effects of time-invariant covariates; all such covariates are effectively removed from the analysis, as is their influence on the associations between the time-varying covariates and the response. However, fixed effects models can estimate interactions between time-invariant and time-varying covariates. For example, although the effect of a time-invariant treatment on the response at any particular occasion cannot be estimated, by including an interaction between treatment and time since baseline we can estimate how treatment effect at a particular occasion differs from that at baseline.

[2]Note that there are several transformations that eliminate α_i from the model, such as subtraction of the baseline values, $Y^*_{ij} = (Y_{ij} - Y_{i1})$ and $X^*_{ijk} = (X_{ijk} - X_{i1k})$ (see Section 8.8); however, in general, mean-centering is the preferred transformation.

9.3 FIXED EFFECTS VERSUS RANDOM EFFECTS: BIAS-VARIANCE TRADE-OFF

As we noted earlier, fixed effects models remove the potential for bias due to certain types of confounding variables, namely measured and unmeasured time-invariant confounders whose effects on the response can be assumed to be constant across measurement occasions. This property is not shared by linear mixed effects models. The linear mixed effects model implicitly makes stronger assumptions about the stable, time-invariant, characteristics of individuals. Specifically, mixed effects models treat the α_i as random, rather than fixed, and assume that they are uncorrelated with the measured covariates included in the regression model; that is, the α_i are assumed to be uncorrelated with X_{ij} (and also uncorrelated with W_i and with ϵ_{ij}). When these assumptions do not hold for the data at hand, and some of the between-subject variation in the α_i includes unmeasured characteristics of subjects that are correlated with the covariates of interest, X_{ij}, then the linear mixed effects model can yield biased estimates of the effects of X_{ij} on Y_{ij}. In contrast, the fixed effects model makes milder assumptions about the stable characteristics of individuals, implicitly allowing for the possibility of correlation between the α_i and X_{ij}. In the fixed effects model the effects of X_{ij} on Y_{ij} are estimated by effectively ignoring all of the between-subject variation and focusing exclusively on the within-subject variation. By focusing only on within-subject variation, we ensure that the α_i cannot possibly have any effect on the estimation of β, regardless of whether they are correlated with X_{ij}. Therefore in the fixed effects model the α_i, representing measured and unmeasured stable characteristics of individuals, cannot confound the estimation of the effects of X_{ij} on Y_{ij}.

Because the fixed effects model has the potential to avoid bias in the estimation of time-varying covariate effects, it may seem that it should always be the method of first choice for longitudinal analysis. However, there are two main reasons why the linear mixed effects model might often be preferred. First, in many longitudinal designs there is scientific interest in the effects of both time-varying and time-invariant covariates. Indeed, in many longitudinal studies the primary covariates of scientific interest are time-invariant, such as fixed treatment or exposure groups, or various background characteristics of individuals (e.g., gender, socioeconomic status). Linear mixed effects models allow for the estimation of the effects of both time-varying and time-invariant covariates; in contrast, fixed effects models cannot estimate the effects of time-invariant covariates. Second, the potential advantage of fixed effects models over mixed effects models in terms of bias in the estimation of the effects of time-varying covariates comes at a price: efficiency. As is quite common in statistical estimation, there is a trade-off between bias and efficiency. Although, under certain conditions, the fixed effects model may provide unbiased estimates of the effects of time-varying covariates, it will in general yield larger standard errors for those estimated effects than those produced by the mixed effects model. The reason is as follows. Recall that a time-varying covariate has two main sources of variation: within-subject variation (i.e., the degree to which values of the covariate vary over time within the same individual) and between-subject variation (i.e., the degree to which values of the covariate vary from one individual to another). In many longitudinal studies the between-subject variation in a time-varying covariate is orders of magnitude greater than the within-subject variation. For example, in a longitudinal study of the effect of body mass index (BMI) on pulmonary function, we might expect to see far greater variation in BMI between individuals than fluctuations in BMI within individuals over the duration of the study. Similarly, in many studies of growth and aging, there may be far greater variation in age between individuals than within individuals over the course of the study. Fixed effects models base estimation exclusively on the within-subject variation and completely ignore the between-subject variation. In contrast, mixed effects models capitalize on both sources of variation, between- and within-subject variation, yielding standard errors that can be substantially smaller. In general, the greater the proportion of variation in a time-varying covariate that is between-subject variation, the larger the difference in the magnitudes of the standard errors yielded by the fixed and mixed effects models.

Thus the choice between fixed and mixed effects models is very often made on a combination of scientific and statistical grounds. On scientific grounds, the choice between these two classes of models is clear-cut when there is scientific interest in the effects of time-invariant covariates. Fixed effects models simply cannot estimate these effects while mixed effects models can. The choice between these two classes of models for the estimation of the effects of time-varying covariates can be made on statistical grounds but requires the balancing of bias versus precision. In settings where there is substantial concern about confounding by stable characteristics of individuals and/or where there is substantial within-subject variation in the time-varying covariate of interest, the fixed effects model will be preferred. Conversely, in settings where most of the major confounding variables have been measured and included in the analysis and/or where the between-subject variation is orders of magnitude larger than the within-subject variation in the time-varying covariate of interest, the mixed effects model will be preferred.

Finally, it is worth mentioning settings where the two approaches are anticipated to yield very similar estimates of effects.† Consider the following simple random effects model, with single covariate X_{ij}:

$$Y_{ij} = \beta_1 + \beta_2 X_{ij} + b_i + \epsilon_{ij}, \tag{9.2}$$

where $b_i \sim N(0, \sigma_b^2)$. Although the technical details are omitted here, the ML estimate of β_2 in this simple random effects model, denoted $\widehat{\beta}_2^{(RE)}$, can be shown to be a weighted average,

$$\widehat{\beta}_2^{(RE)} = (1-w)\,\widehat{\beta}_2^{(FE)} + w\,\widehat{\beta}_2^{(B)}, \tag{9.3}$$

†The remainder of this section can be skipped on a first reading. However, the reader who returns to it will find that it yields insights about when the fixed and mixed effects estimators are likely to be similar.

where $\widehat{\beta}_2^{(B)}$ is obtained from the regression of $\overline{Y}_i$ on $\overline{X}_i$ and is based only on the between-subject variation in the response and covariate. Recall that in contrast to $\widehat{\beta}_2^{(B)}$, $\widehat{\beta}_2^{(FE)}$ is based only on the within-subject variation in the response and covariate. Thus this simple expression demonstrates that the ML estimate of β_2 is based on an optimal weighted combination of the within-subject and between-subject sources of variation in the response and covariate. The actual weight, w, is determined by the equation,

$$w = \frac{(1-\rho_y)\rho_x}{(1-\rho_y) + n\rho_y(1-\rho_x)}, \tag{9.4}$$

where $\rho_y = \frac{\sigma_b^2}{\sigma_b^2+\sigma_\epsilon^2}$ is the proportion of variability in the response that is due to between-subject variation, and ρ_x is the corresponding proportion of variability in the covariate that is due to between-subject variation. From (9.3) it is apparent that when $w \approx 0$, we expect $\widehat{\beta}_2^{(RE)} \approx \widehat{\beta}_2^{(FE)}$; conversely, when $w \neq 0$, we expect $\widehat{\beta}_2^{(RE)}$ to differ from $\widehat{\beta}_2^{(FE)}$, unless $\widehat{\beta}_2^{(FE)} \approx \widehat{\beta}_2^{(B)}$. Further examination of the expression for w given by (9.4) reveals when w is expected to be small. First, for a fixed value of ρ_x, w is expected to be small when ρ_y is large, such as when $\rho_y \longrightarrow 1$, $w \longrightarrow 0$. Thus $\widehat{\beta}_2^{(RE)} \approx \widehat{\beta}_2^{(FE)}$ when the between-subject variation in the *response* is large relative to the within-subject variation. For example, the two approaches are anticipated to yield very similar estimates of effects when the pairwise correlation among repeated measures is large and close to one. Put another way, when the within-subject variation in the *response* is relatively small the repeated measures on an individual are highly reliable. Therefore the most precise estimate of β_2 is obtained by relying more heavily on how changes in the covariate are associated with changes in the response *within the same subject*. Second, w is expected to be small when ρ_x is small, such as when $\rho_x \longrightarrow 0$, $w \longrightarrow 0$. Thus $\widehat{\beta}_2^{(RE)} \approx \widehat{\beta}_2^{(FE)}$ when the within-subject variation in the *covariate* is large relative to the between-subject variation in the covariate. For example, in many designed longitudinal studies there are covariates that vary systematically over time but are fixed by design of the study. In many of these studies $X_{ij} = X_j$ for all subjects, e.g., X_j might denote time since baseline when the measurement occasions are fixed by the study design. This implies that all of the variation in the covariate is within-subject variation and $\rho_x = 0$. Another closely related example arises in crossover study designs where X_{ij} is a treatment group indicator denoting the treatment received by the i^{th} subject at the j^{th} occasion. In many classical crossover designs, each subject receives all of the treatments being compared but in a random sequence or order (see Chapter 21). For these classical crossover study designs, $\overline{X}_i = \overline{X}$ for all subjects, which implies that all of the variation in the covariate is within-subject variation ($\rho_x = 0$). Finally, examination of (9.4) reveals that when the number of repeated measures, n (here assumed to be equal for all subjects), is large, then w will tend to be small. So, in longitudinal studies with a very large number of repeated measurements, $\widehat{\beta}_2^{(RE)}$ and $\widehat{\beta}_2^{(FE)}$ are expected to be similar.

9.4 RESOLVING THE DILEMMA OF CHOOSING BETWEEN FIXED AND RANDOM EFFECTS MODELS

Fixed and random effects models yield estimators of the effects of time-varying covariates with different desirable properties. Much of the statistical literature comparing these two alternative approaches presents them as mutually exclusive choices; that is, one must choose between the two types of models, making a choice between the potential bias associated with the random effects model formulation and the increased sampling variability associated with the fixed effects model formulation. However, there is a third option, albeit one that does not appear to have been so widely adopted in practice: develop a model that capitalizes on most of the appealing features of both the random and fixed effects model formulations. Specifically, it is possible to specify a linear mixed effects model that explicitly allows, when it is deemed necessary, separate estimation of the effect of a time-varying covariate from the two distinct sources of variation in that covariate: one estimate based exclusively on within-subject variation in the response and covariate, the other estimate based exclusively on between-subject variation in the response and covariate. Indeed, it is possible to calculate these estimates for any subset of the time-varying covariates. Such a model recognizes that longitudinal data can provide two distinct sources of information about the relationship between a time-varying covariate and the response: (1) between-subject information reflected in the fact that, at any occasion, different individuals have different values of the covariate and response, and (2) within-subject information reflected in the fact that the covariate and response change over time within subjects. These can be thought of as "cross-sectional" and "longitudinal" information, respectively. Such a model also recognizes that these two sources of information can potentially provide conflicting signals about the nature and magnitude of the covariate effect; the latter is highlighted with a graphical illustration in Section 9.5.

In the standard linear mixed effects model, the estimated effect of a time-varying covariate is based on an optimal combination of the within-subject and between-subject variation. However, when the longitudinal and cross-sectional information are in conflict, these two sources of information should not be combined. Conversely, when they are not in conflict, it is advantageous to optimally combine them to yield the most precise estimate of the covariate effect. These are the principles that guide the specification of a linear mixed effects model that explicitly allows, when necessary, for separate estimation of the effects of time-varying covariates based exclusively on the within- or the between-subject variation in the response and covariates. That is, the model makes an appropriate decomposition of between- and within-subject effects. The case for such a model formulation is at least fivefold:

1. The model allows for joint estimation of the effects of both time-varying and time-invariant covariates, thereby overcoming an important limitation of the fixed effects model.

2. By including a vector of random effects, the model allows for heterogeneity in the effects of certain time-varying covariates and a more flexible model for the marginal covariance among the repeated measures of the response.

3. The model allows separate estimation of the effects of time-varying covariates based on within- and between-subject variation. The resulting estimator based on the within-subject variation shares all of the desirable properties of the fixed effects estimator, i.e., the estimator is unbiased even when b_i is correlated with a time-varying covariate.

4. The model allows for a formal statistical comparison of the estimates based on the within-subject and between-subject variation. Moreover, when there is sufficient evidence that they are not discernibly different, a combined estimate based on both sources of variation can be obtained; the resulting estimator shares the desirable property with the random effects estimator of being more efficient than the fixed effects estimator.

5. Finally, maximum likelihood estimation of the covariate effects within a linear mixed effects model yields valid inferences when data are missing at random (MAR), but not necessarily missing completely at random (MCAR); see Section 4.3 for the definitions of, and the distinction between, MCAR and MAR. In contrast, OLS estimation of fixed effects models can produce biased estimates of covariate effects when data are MAR.

This approach, combining the appealing features of both the fixed and random effects formulation without any of the major limitations of either approach, provides a more attractive option than having to choose between adopting either a fixed or random effects model.

Next we outline the specification of this model. Following the notation introduced earlier, we let X_{ij} denote the $q \times 1$ vector of time-varying covariates and W_i denote the $(p - q) \times 1$ vector of time-invariant covariates. We denote the mean-centered covariates by X^*_{ijk}, where $X^*_{ijk} = X_{ijk} - \overline{X}_{ik}$, for $k = 1, ..., q$. The mean-centered covariates can be grouped together in a $q \times 1$ vector denoted by X^*_{ij}; similarly the means of the covariates can be grouped together in a $q \times 1$ vector denoted by $\overline{X}_i$. The linear mixed effects model that allows for simultaneously estimating cross-sectional and longitudinal effects of X_{ij} on Y_{ij} is then given by

$$Y_{ij} = X^{*\prime}_{ij}\beta^{(L)} + \overline{X}'_i\beta^{(C)} + W'_i\gamma + Z'_{ij}b_i + \epsilon_{ij}, \tag{9.5}$$

where b_i is a vector of random effects, with $b_i \sim N(0, G)$, Z_{ij} is the design vector for the random effects and is a subset of the components of X_{ij}, and $\epsilon_{ij} \sim N(0, \sigma^2_\epsilon)$. Note that the inclusion of a vector of random effects, b_i, allows for heterogeneity in the effects of certain time-varying covariates and a flexible model for the marginal covariance among the repeated measures of the response (see Section 8.3).

This model allows both cross-sectional effects, $\beta^{(C)}$, and longitudinal effects, $\beta^{(L)}$, to be modeled simultaneously. The interpretation of the model parameters, $\beta^{(C)}$ and $\beta^{(L)}$, becomes more transparent when the implied models for the average response (where averaging is over time) and within-subject changes in the response are considered. First, consider the model for the time-averaged response, $\overline{Y}_i = \frac{1}{n_i}\sum_{j=1}^{n_i} Y_{ij}$,

$$\overline{Y}_i = \overline{X}'_i\beta^{(C)} + W'_i\gamma + e_i,$$

where $e_i = \frac{1}{n_i}\sum_{j=1}^{n_i}(Z'_{ij}b_i + \epsilon_{ij}) = \overline{Z}'_i b_i + \overline{\epsilon}_i$. The regression parameters $\beta^{(C)}$ represent the cross-sectional effects of X_{ij} when different individuals having distinct average values for X_{ij} are compared and contrasted. Next consider the model for within-subject changes, say $Y_{ij} - Y_{i1}$. The model for the within-subject changes is given by

$$\begin{aligned} Y_{ij} - Y_{i1} &= X^{*\prime}_{ij}\beta^{(L)} + \overline{X}'_i\beta^{(C)} + W'_i\gamma + Z'_{ij}b_i + \epsilon_{ij} \\ &\quad -(X^{*\prime}_{i1}\beta^{(L)} + \overline{X}'_i\beta^{(C)} + W'_i\gamma + Z'_{i1}b_i + \epsilon_{i1}) \\ &= (X'_{ij} - X'_{i1})\beta^{(L)} + (Z'_{ij} - Z'_{i1})b_i + (\epsilon_{ij} - \epsilon_{i1}) \\ &= (X'_{ij} - X'_{i1})\beta^{(L)} + e_{ij}, \end{aligned}$$

where $e_{ij} = (Z'_{ij} - Z'_{i1})b_i + (\epsilon_{ij} - \epsilon_{i1})$. Therefore, in the model for the within-subject changes, $\beta^{(L)}$ represents a vector of regression parameters for longitudinal effects of X_{ij}, describing how within-subject changes in the covariates are related to within-subject changes in the response. Note that when it is assumed that the cross-sectional and longitudinal effects of X_{ij} are the same, so that $\beta^{(C)} = \beta^{(L)} = \beta$, the model given by (9.5) collapses to the standard linear mixed effects model,

$$\begin{aligned} Y_{ij} &= X^{*\prime}_{ij}\beta^{(L)} + \overline{X}'_i\beta^{(C)} + W'_i\gamma + Z'_{ij}b_i + \epsilon_{ij} \\ &= X^{*\prime}_{ij}\beta + \overline{X}'_i\beta + W'_i\gamma + Z'_{ij}b_i + \epsilon_{ij} \\ &= \left(X'_{ij}\beta - \overline{X}'_i\beta\right) + \overline{X}'_i\beta + W'_i\gamma + Z'_{ij}b_i + \epsilon_{ij} \\ &= X'_{ij}\beta + W'_i\gamma + Z'_{ij}b_i + \epsilon_{ij}. \end{aligned}$$

One important advantage of simultaneously modeling cross-sectional and longitudinal effects is that formal comparisons can be made by testing H_0: $\beta^{(C)} = \beta^{(L)}$ (or by comparing certain components of $\beta^{(C)}$ with the corresponding components of $\beta^{(L)}$). In the econometrics literature, the comparison of the estimates of the effects of time-varying covariates from fixed and random effects models is known as the "Hausman test" (Hausman, 1976). The Hausman test is often presented as a classical test of whether the fixed or random effects model should be used. However, as noted earlier, in many longitudinal designs there is scientific interest in both the effects of time-varying covariates and time-invariant covariates (e.g., fixed treatment or exposure groups). In these settings the fixed effects model is not appealing because it precludes the estimation of the effects of time-invariant covariates. On the other hand, it is of interest to compare the cross-sectional and longitudinal effects of time-varying covariates because the longitudinal effects are not prone to confounding by measured and unmeasured stable characteristics of individuals.

The testing of H_0: $\beta^{(C)} = \beta^{(L)}$ in the linear mixed effects model is very similar in spirit to the Hausman test. However, within this modeling framework we can also consider a much broader range of tests, such as tests of equality of subsets of the components of $\beta^{(C)}$ and $\beta^{(L)}$. In cases where there is insufficient evidence that certain components of $\beta^{(C)}$ and $\beta^{(L)}$ differ, we can obtain a single estimate from the linear mixed effects model that is based on the optimal combination of the between-subject (or cross-sectional) and within-subject (or longitudinal) sources of variation. Moreover the model allows for estimation of the effects of time-invariant covariates, γ, regardless of whether it is assumed that $\beta^{(C)} = \beta^{(L)}$.

9.5 LONGITUDINAL AND CROSS-SECTIONAL INFORMATION

In this section we highlight how the two sources of information for a time-varying covariate, longitudinal (or within-subject) and cross-sectional (or between-subject), can potentially provide conflicting signals about the nature and magnitude of the covariate effect. To fix ideas, consider a study of aging. In Chapter 1, when we discussed the main distinctions between a longitudinal and cross-sectional study, we emphasized that the assessment of within-subject changes in the response due to aging can only be achieved within a longitudinal study design. In a cross-sectional study, where the response is measured at a single occasion, we cannot estimate the effect of aging (an inherently within-subject effect); instead, we can only make comparisons among sub-populations that happen to differ in age. However, when the effect of aging is determined from a cross-sectional study, there is the danger that it is potentially confounded with cohort effects.

When an initial cross-sectional sample is measured repeatedly through time, it is then possible to make comparisons of longitudinal and cross-sectional estimates of changes in the response. For example, the Muscatine Coronary Risk Factor (MCRF) study enrolled five cohorts of children, initially aged 5–7, 7–9, 9–11, 11–13, and 13–15 years. Repeated measurements of obesity, based on BMI, were obtained biennially, from 1977 to 1981, with the objective of determining whether the risk of obesity increased with age. Note that the data from the MCRF study are unbalanced over time when the age of the child is used as the metameter for time. That is, baseline measurements are taken at the same calendar time (1977) for all subjects but age at entry to the study varies with subjects. As a result there are two potential sources of information about changes in BMI with age. First, there is cross-sectional or between-subject information about how BMI changes with age in the baseline observations obtained in 1977, since children enter the study at different ages. Similar cross-sectional information is also available in 1979 and 1981 (or, equivalently, in the average of the repeated measures over time). Second, longitudinal or within-subject information arises because children are measured repeatedly over time, yielding measurements of BMI at different ages. These two sources of information may provide conflicting information about how BMI changes with age.

As we discussed in previous sections, when a study provides both longitudinal and cross-sectional information, somewhat greater care must be exercised in specifying models for the response to avoid confounding of longitudinal effects with cross-sectional effects. The linear mixed effects model presented in Section 9.4 includes separate parameters that represent the cross-sectional and longitudinal effects of age on the response and allows simultaneous estimation of both types of effects. This makes it possible to compare the cross-sectional and longitudinal effects, and to report separate effects where necessary, or estimate a combined effect, based on both sources of information, if appropriate.

In a small departure from the notation used in the previous section, we let Age_{ij} denote the age of the i^{th} subject at the j^{th} measurement occasion. A model for aging, with decomposition of between- and within-subject effects, is given by

$$Y_{ij} = \beta_1 + \beta_2^{(L)}(\text{Age}_{ij} - \overline{\text{Age}}_i) + \beta_2^{(C)}\overline{\text{Age}}_i + W_i'\gamma + b_{1i} + b_{2i}\text{Age}_{ij} + \epsilon_{ij},$$

where $\beta_2^{(C)}$ represents the cross-sectional effect of age since it describes how the mean response at any occasion varies with age at that occasion. In contrast, $\beta_2^{(L)}$ represents the longitudinal effect of age since it describes how within-subject changes in the response are related to within-subject changes in age. Differences between $\beta_2^{(C)}$ and $\beta_2^{(L)}$ can arise when there are cohort or period effects. Cohort effects will introduce bias in the cross-sectional estimate but not the longitudinal estimate. Period effects will introduce bias in the longitudinal estimate but not the cross-sectional estimate. Alternatively, differences between $\beta_2^{(C)}$ and $\beta_2^{(L)}$ can be due to the biasing effects of selective dropouts. When $\beta_2^{(C)} = \beta_2^{(L)} = \beta_2$, the model given above simplifies to

$$Y_{ij} = \beta_1 + \beta_2\text{Age}_{ij} + W_i'\gamma + b_{1i} + b_{2i}\text{Age}_{ij} + \epsilon_{ij},$$

the standard linear mixed effects model. On the other hand, when $\beta_2^{(C)} \neq \beta_2^{(L)}$ but the model for the data does not allow for separate estimation of the cross-sectional and longitudinal effects on the response, then β_2 cannot be interpreted as a pure longitudinal effect of aging. Instead, β_2 is some weighted combination of $\beta_2^{(C)}$ and $\beta_2^{(L)}$, with weights determined by the relative magnitudes of the between- and within-subject variation (see equations (9.3) and (9.4) in Section 9.3). Such a weighted combination of $\beta_2^{(C)}$ and $\beta_2^{(L)}$ may not reflect an effect of subject-matter interest. That is, failure to distinguish between cross-sectional and longitudinal effects can result in a distorted estimate of the effect of age that reflects neither the cross-sectional nor the longitudinal effect of age on the response.

Illustration

The main distinction between cross-sectional and longitudinal effects is highlighted in the following simple illustration. Suppose that three age-cohorts of children, initially aged 5, 6, and 7 years, are measured at baseline and followed annually for three years. Suppose that the cross-sectional effect of age on the response is linear, with

$$E(\overline{Y}_i) = \beta^{(C)}\overline{\text{Age}}_i$$

(for simplicity, a model with intercept equal to zero is assumed). The same cross-sectional relationship, with slope $\beta^{(C)}$, is assumed to hold at every measurement occasion. The mean response is also assumed to increase linearly with changes in age in each cohort

$$E(Y_{ij} - \overline{Y}_i) = \beta^{(L)}(\text{Age}_{ij} - \overline{\text{Age}}_i),$$

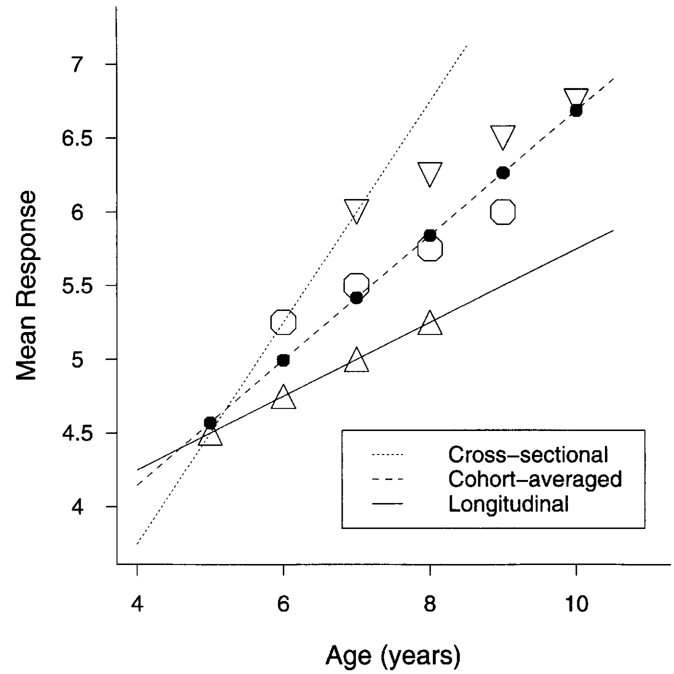

Fig. 9.1 Plot of the longitudinal, cross-sectional, and cohort-averaged regression lines for the three age-cohorts: $\triangle$ denotes mean response of the age-cohort of children initially aged 5 years; $\bigcirc$ denotes mean response of the age-cohort of children initially aged 6 years; and ∇ denotes mean response of the age-cohort of children initially aged 7 years. ($\bullet$ denotes mean response when averaged over the three age cohorts).

but with slope $\beta^{(L)} \neq \beta^{(C)}$. Thus in this model $\beta^{(C)}$ represents the cross-sectional effect of age, whereas $\beta^{(L)}$ represents the longitudinal effect of age.

A graphical representation of this model for the mean response versus age, with $\beta^{(C)} = 0.75$ and $\beta^{(L)} = 0.25$, is given in Figure 9.1. In this illustration there is a discernible difference between the longitudinal (solid line) and cross-sectional (dotted line) effects of aging on the mean response. When these differences between the longitudinal and cross-sectional effects of aging are ignored, the observed changes in the mean response with age of measurement (see dashed line in Figure 9.1) reflect a weighted combination of $\beta^{(C)}$ and $\beta^{(L)}$. Recall from equation (9.3) that the ML estimate from the naive analysis assuming $\beta^{(C)} = \beta^{(L)} = \beta$ is the following weighted average:

$$\widehat{\beta} = (1 - w)\,\widehat{\beta}^{(L)} + w\,\widehat{\beta}^{(C)},$$

where

$$w = \frac{(1 - \rho_y)\rho_x}{(1 - \rho_y) + n\rho_y(1 - \rho_x)}.$$

Here $n = 4$ and ρ_x denotes the proportion of variability in age due to between-subject variation relative to within-subject variation. In this illustration, approximately 35% of the variation is due to between-subject variation and 65% is due to within-subject variation ($\rho_x = 0.3478$). For this study design, with n and ρ_x fixed by design, the resulting estimate of β depends on the magnitude of ρ_y, the correlation among the repeated measures of the response. Specifically, the estimate of β can range from 0.25 (when $\rho_y = 1$ and $w = 0$) to 0.424 (when $\rho_y = 0$ and $w = 0.3478$). The dashed line in Figure 9.1 depicts the case where $\rho_y = 0$. In general, when differences between the longitudinal and cross-sectional effects are ignored, the naive analysis assuming $\beta^{(C)} = \beta^{(L)} = \beta$ estimates a weighted average of $\beta^{(C)}$ and $\beta^{(L)}$.

This simple illustration highlights why standard regression models for longitudinal data that do not incorporate separate cross-sectional and longitudinal effects of time-varying covariates can potentially yield misleading inferences. That is, failure to acknowledge that the cross-sectional effect differs from the longitudinal effect can lead to a conclusion about the effect of the covariate that confounds one effect with the other.

9.6 CASE STUDY

Next we illustrate the main ideas presented in this chapter using lung function growth data on a randomly selected subset of female participants from the Six Cities Study of Air Pollution and Health. The random sample consists of 300 girls from Topeka, Kansas, one of the participating cities in the study. Each girl had a minimum of 1 and a maximum of 12 measurements of FEV_1, height and age over the course of the study. One outlying observation was removed and all analyses are based on the data from 299 girls (with a total of 1993 measurements).

The goal of the analysis is to assess the relationship between FEV_1 and age. There are two sources of information about the relationship between FEV_1 and age. First, there is "cross-sectional" or between-subject information that arises from the comparison of children of different ages. Second, there is "longitudinal" or within-subject information that arises because children are measured repeatedly over time, yielding measurements of FEV_1 at different ages.

We begin with a so-called fixed effects analysis of these data. Recall that the fixed effects analysis focuses exclusively on the "longitudinal" information about the relationship between FEV_1 and age. To adjust for variation in a child's stature, values for FEV_1 were divided by height squared and log-transformed; this has been shown to be an effective yet parsimonious adjustment for height. We consider the following fixed effects model for log(FEV_1/height^2):

$$E(Y_{ij}) = \beta_1 + \beta_2 \text{Age}_{ij} + \alpha_i,$$

where Y_{ij} is the log(FEV_1/height^2) for the i^{th} child at the j^{th} occasion, Age_{ij} is the age for the i^{th} child at the j^{th} occasion, and α_i are fixed effects representing stable (i.e., time-invariant) characteristics of the children. Because the model includes an

Table 9.1 Regression estimates and standard errors for the fixed effects model for the $\log(\text{FEV}_1/\text{height}^2)$ data from the Six Cities Study.

Variable	Estimate	SE	Z
ID 1	−0.399	0.0252	−15.81
ID 2	−0.302	0.0238	−12.72
ID 3	−0.243	0.0223	−10.91
⋮	⋮	⋮	⋮
Age (×100)	2.982	0.0480	62.15

Table 9.2 Regression (and variance) estimates and standard errors for the random effects model for the $\log(\text{FEV}_1/\text{height}^2)$ data from the Six Cities Study.

Variable	Estimate	SE	Z
Intercept	−0.355	0.0082	−43.42
Age (×100)	2.981	0.0473	62.99
σ_b^2 (×100)	0.931	0.0849	
σ_ϵ^2 (×100)	0.419	0.0144	

intercept, β_1, 298 dummy or indicator variables must be included in the model to estimate the α_i. In this model, β_2 is the "longitudinal" effect of age. Estimates of β_1, β_2, and α_i can be obtained, via ordinary least squares (OLS), using any standard linear regression software. The results from fitting this fixed effects model are reported in Table 9.1. These result indicate that there is a significant effect of age. The estimated coefficient for age, 0.0298, indicates that each one year increase in age is associated with an $e^{0.0298} = 1.030$ or 3.0% relative increase in FEV_1 (adjusted for height^2). Also reported in Table 9.1 are the estimates of the subject-specific effects $(\beta_1 + \alpha_i)$ for the first three subjects in the sample.

Next we consider a similar analysis of these data where the α_i are no longer fixed but are considered to be random; to emphasize this distinction, the subject-specific effects are now denoted b_i,

$$E(Y_{ij}|b_i) = \beta_1 + \beta_2 \text{Age}_{ij} + b_i,$$

where $b_i \sim N(0, \sigma_b^2)$. The results from fitting the random effects model are reported in Table 9.2 and are remarkably similar to those for the fixed effects model. The estimated coefficient for age, 0.0298, indicates that each one year increase in age is associated with a 3.0% relative increase in FEV_1 (adjusted for height^2). The congruence between the estimates of the effect of age from the fixed and random effects models suggests that any omitted time-invariant characteristics of the children are likely uncorrelated with age and/or that the random effects estimate is primarily based on the within-subject variation. This congruence can be explained by considering the relative magnitudes of the between- and within-subject sources of variation in these data. For age, 17.2% of the variation is between-subject variation and $\widehat{\rho}_x = 0.172$. For the response, 69% of the variation is between-subject variation, with $\widehat{\rho}_y = \frac{0.931}{0.931+0.419} = 0.69$. Recall from equation (9.3) that the random effects approach is based on an optimal weighted combination of the within-subject and between-subject sources of variation in the response and covariate. As was discussed in Section 9.3, the fixed and random effects approaches yield similar estimates when the weight,

$$w = \frac{(1-\rho_y)\rho_x}{(1-\rho_y) + n\rho_y(1-\rho_x)},$$

is small and close to zero. For the lung function growth data,

$$w \approx \frac{(1-\rho_y)\rho_x}{(1-\rho_y) + \overline{n}\rho_y(1-\rho_x)} = \frac{(1-0.69)\times 0.172}{(1-0.69) + 6.67\times 0.69\times(1-0.172)} = 0.013,$$

where $\overline{n} = \frac{1}{N}\sum_{i=1}^{N} n_i = 6.67$. This implies that the estimated effect of age from the random effects model gives approximately 99% of the weight to the fixed effects estimate; that is, estimation of the effect of age is based almost entirely on the within-subject variation in the response and covariate. Although there is some discernible between-subject variation in age (approximately 1/5 of the variation) in these data, its importance for estimation of the effect of age is almost completely downweighted by the magnitude of ρ_y (the proportion of between-subject variation in the response). Thus, in this instance, the random effects model is a very close approximation to the fixed effects model. Therefore it should not be too surprising that they yield similar estimates of effects and also very similar standard errors. However, we caution that this similarity in estimates between the fixed and random effects models cannot be expected in general.

Although there is almost perfect congruence between the fixed and random effects models for these data, for illustrative purposes we consider a mixed effects model that allows for separate estimation of the effect of age from the between- and within-subject sources of information. The model is

$$E(Y_{ij}|b_i) = \beta_1 + \beta_2^{(L)}(\text{Age}_{ij} - \overline{\text{Age}}_i) + \beta_2^{(C)}\overline{\text{Age}}_i + b_i,$$

where $b_i \sim N(0, \sigma_b^2)$. This analysis yields $\widehat{\beta}_2^{(L)}(\times 100) = 2.982$ (SE = 0.0480) and $\widehat{\beta}_2^{(C)}(\times 100) = 2.923$ (SE = 0.2901). A formal comparison of these two estimates of the effect of age, testing H_0: $\beta_2^{(L)} = \beta_2^{(C)}$, produces a chi-squared statistic of 0.04, with 1 df, $p > 0.80$. Thus there is no evidence of any conflict between the longitudinal and cross-sectional information. This provides additional justification for the combined estimate of the effect of age from the mixed effects model analysis reported in Table 9.2. Finally, we note that the mixed effects model analysis can be extended in a natural way to allow for randomly varying intercepts and slopes. This allows for a more flexible model for the marginal covariance among the repeated measures of the response (see Section 8.3). Although the addition of randomly varying slopes leads to a discernible improvement in the fit of the model to these data, the results of such an analysis yields an estimate of the effect of age ($\times 100$) of 3.010 (SE = 0.0661) that is very similar to that reported in Table 9.2. However, we note that the standard error is approximately 40% larger and may provide a more realistic estimate of the true sampling variability.

9.7 COMPUTING: FITTING LINEAR FIXED EFFECTS MODELS USING PROC GLM IN SAS

To fit linear fixed effects models, we can use PROC GLM in SAS. The GLM procedure fits general linear models using ordinary least squares (OLS) or maximum likelihood estimation under the assumption of normal errors. To fit a fixed effects model, dummy or indicator variables for subjects must be included in the model to jointly estimate β and the α_i. Linear regression with indicator variables for subjects yields the same estimate of β that would be obtained from the OLS regression of the *mean-centered* response and covariates.

In a regression model that includes an intercept term, say β_1, $N - 1$ indicator variables must be included (where N denotes the number of subjects). That is, we include an indicator variable for each subject except the last; the last subject then becomes the "reference." These indicator variables can be created automatically by including the subject identifier on the CLASS statement in PROC GLM. Alternatively, in a regression model that omits an intercept term, N indicator variables must be included. These indicator variables can also be created automatically by including the subject identifier on the CLASS statement in PROC GLM. One small advantage of the latter approach is that the N subject-specific effects (the α_i's) are directly estimated. In the former approach, the subject-specific effect for the last subject (the "reference") is β_1, while the subject-specific effects for the remaining subjects are $\beta_1 + \alpha_i$ $(i = 1, ..., N - 1)$. There is ordinarily little interest in the subject-specific effects; they are regarded as nuisance parameters in the fixed effects model formulation.

We note that estimation of N subject-specific effects increases the computations required for fitting the fixed effects model. This may be of concern in studies where N is very large. Fortunately, it is possible to reduce this computational burden by not explicitly estimating the N subject-specific effects; instead, only the covariate effects are estimated. Without explaining the technical details, this is achieved by removing the subject identifier from the MODEL and CLASS statements and including the subject identifier on the ABSORB statement instead. This will yield identical estimates (and standard errors) of the covariate effects but greatly reduce the computation time. The only practical difference in the output is that no estimates of the subject-specific

Table 9.3 Illustrative commands for fixed effects model using PROC GLM in SAS.

```
PROC GLM;
    CLASS  id;
    MODEL  y=age id / SOLUTION;
```

Table 9.4 Illustrative commands for fixed effects model using the ABSORB statement in PROC GLM in SAS.

```
PROC GLM;
    ABSORB  id;
    MODEL  y=age / SOLUTION;
```

effects are produced. As mentioned earlier, this is usually not a concern as they are regarded as nuisance parameters in the fixed effects model.

For example, to fit a fixed effects model to longitudinal data from a study of aging, we can use the illustrative SAS commands given in Tables 9.3 and 9.4. Next we present a brief description of the most salient parts of the command syntax used in the illustrations in Tables 9.3 and 9.4.

PROC GLM <options>;

This statement calls the procedure GLM in SAS. PROC GLM is a very versatile procedure for fitting general linear models, including standard linear regression and ANOVA models.

CLASS variables;

The CLASS statement is used to identify all variables that are to be treated as categorical. By default, this statement will create indicator variables for each listed variable using a reference group coding, with the last level (where "last" refers to the level with the largest alphanumeric value) treated as the reference group. In Table 9.3, the subject identifier, `id`, is listed on the CLASS statement and this automatically yields $N - 1$ indicator variables (where N denotes the number of subjects) when the subject identifier, `id`, is also included as a covariate in the MODEL statement in PROC GLM.

ABSORB variables;

When a variable is included in the ABSORB statement, the effect of that variable is removed before the construction and solution of the remainder of the

model. Absorption can provide a large reduction in computer time and memory requirements, especially when the absorbed effect has a large number of levels. In Table 9.4 the subject identifier, `id`, is listed on the ABSORB statement. This avoids the explicit estimation of the subject-specific effects, α_i, in the fixed effects model. As a result it is no longer necessary to include the subject identifier, `id`, in the MODEL statement.
Note: The data set must be sorted by the variable(s) in the ABSORB statement.

MODEL response = <effects> / <options>;
The MODEL statement specifies the response variable and the covariate effects. The covariate effects can include both discrete (defined in the CLASS statement) and quantitative (excluded from the CLASS statement) covariates. By default, PROC GLM includes a column of 1's for the intercept in the model. In Table 9.3 the MODEL statement includes `age` as a time-varying quantitative (excluded from the CLASS statement) covariate and `id` as a discrete (defined in the CLASS statement) covariate or factor. Because id is included in the CLASS statement in Table 9.3, this automatically yields $N - 1$ indicator variables (where N denotes the number of subjects) for the subject-specific effects. In Table 9.4 the MODEL statement only includes `age` as a time-varying quantitative (excluded from the CLASS statement) covariate. Because id is included in the ABSORB statement in Table 9.4, explicit estimation of the subject-specific effects, α_i, is avoided.

9.8 COMPUTING: DECOMPOSITION OF BETWEEN-SUBJECT AND WITHIN-SUBJECT EFFECTS USING PROC MIXED IN SAS

To fit the linear mixed effects model described in Section 9.4, we can use PROC MIXED in SAS. To allow for simultaneous estimation of both the cross-sectional and longitudinal effects of a time-varying covariate, we simply include both the mean of the covariate (averaged over time) and the mean-centered covariate in the analysis. The estimated coefficient for the mean of the covariate yields an estimate of the cross-sectional effect. The estimated coefficient for the mean-centered covariate yields an estimate of the longitudinal effect. Fitting linear mixed effects models that decompose between-subject and within-subject effects is only slightly more complicated than fitting standard linear mixed effects models.

For example, to fit a mixed effects model to longitudinal data from a study of aging, we can use the illustrative SAS commands given in Table 9.5. In this illustration we estimate both the cross-sectional and longitudinal effects of aging and also the effect of gender, a time-invariant covariate. Recall that the fixed effects model precludes estimation of the effects of any time-invariant covariates.

The first part of the command syntax used in the illustration in Table 9.5 is for the calculation of the mean of the time-varying covariate, `age`. The PROC MEANS procedure in SAS (with the NWAY option) can be used to calculate the mean age for each subject, where averaging is over repeated observations within a subject. Using

Table 9.5 Illustrative commands for decomposition of between- and within-subject effects using PROC MIXED in SAS.

```
PROC MEANS DATA=one NWAY;
    CLASS  id;
    VAR  age;
    OUTPUT OUT=two MEAN=mage;

PROC SORT DATA=one;
    BY  id;

PROC SORT DATA=two;
    BY  id;

DATA three;
    MERGE  one two;
    BY  id;
    cage=age-mage;
RUN;

PROC MIXED DATA=three;
    CLASS  id gender;
    MODEL  y=gender cage mage / SOLUTION;
    RANDOM  INTERCEPT / SUBJECT=id;
```

an OUTPUT statement, the mean age, denoted `mage` in Table 9.5, is written to a second SAS data-set (two). The original SAS data-set (one) and the second SAS data-set (two) are then sorted according to the subject-identifier, `id`. Finally, a third SAS data-set (three) is created by merging these two data-sets. Using the third SAS data-set (three) the mean-centered age variable, denoted `cage` in Table 9.5,

$$\texttt{cage} = \texttt{age} - \texttt{mage},$$

is calculated for each observation. The mean age and mean-centered age variables are then used as covariates in the mixed effects model analysis.

The second part of the command syntax used in the illustration in Table 9.5 is for the fitting of a random effects (random intercepts only) model that includes the effect of gender and both cross-sectional and longitudinal effects of age. Using a CONTRAST statement, the cross-sectional and longitudinal estimates of the effects of aging can be compared.

9.9 FURTHER READING

Allison (2005) provides a remarkably clear and well-organized guide to fixed effects models for longitudinal data, with numerous examples of how to implement the methods using standard statistical software. Ware et al. (1990) present an accessible discussion of regression models for longitudinal data that incorporate separate parameters for cross-sectional and longitudinal effects of aging; also see discussion of discrepancies between longitudinal and cross-sectional effects in Louis et al. (1986). Neuhaus and Kalbfleisch (1998) and Neuhaus (2001) discuss similar issues in the broader context of cluster-correlated data; also see Berlin et al. (1999) and Begg and Parides (2003) for a discussion of the decomposition of between- and within-cluster effects in the analysis of cluster-correlated data.

Bibliographic Notes

The derivation of the "Hausman test" is described in detail in Hausman (1976). Because a very similar approach was first proposed by Durbin (1954), and separately by Wu (1973), tests based on the comparison of two sets of parameter estimates are also referred to as "Durbin–Wu–Hausman" tests.

The statistical basis for the weights in equations (9.3) and (9.4) is discussed in Scott and Holt (1982); a closely related expression for the weights applied to the between-subject and within-subject estimators can also be found in an influential paper in the econometrics literature by Maddala (1971).

Problems

9.1 In a U.S. Centers for Disease Control (CDC) study, conducted in the state of Georgia from 1980 to 1992, linked data on live births to the same mother were obtained (Adams et al., 1997). We focus on a subset of data restricted to 878 mothers for whom five births were identified; these data are from Neuhaus and Kalbfleisch (1998) and are reported in Pan (2002) and Rabe-Hesketh and Skrondal (2008). The main objective of the analysis is to determine the effect of maternal age (the mother's age at each birth) on infant birth weight. Note that because each mother had five infant births, but at different maternal ages, maternal age is a within-subject or time-varying covariate.

The raw data are stored in an external file: `birthwt.dat`

Each row of the data set contains the following five variables:

MID Order Wt Age CID

Note: The outcome variable Wt records the infant birth weight measured in grams. The variable Order denotes the infant birth order (coded 1–5). The variable Age is the mother's age (in years) at each of the five recorded births. Finally, the variables MID and CID denote the mother and child identifiers (IDs).

9.1.1 Let Y_{ij} denote the birth weight (in grams) of the j^{th} infant from the i^{th} mother and Age_{ij} denote the i^{th} mother's age at the time of the birth of her j^{th} infant (for $i = 1, ..., 878; j = 1, ..., 5$). Fit the following standard mixed effects model with linear trend for maternal age and randomly varying intercepts,

$$Y_{ij} = \beta_1 + \beta_2 \text{Age}_{ij} + b_i + \epsilon_{ij},$$

where $b_i \sim N(0, \sigma_b^2)$ and $\epsilon_{ij} \sim N(0, \sigma_\epsilon^2)$.

9.1.2 From the results of the analysis for Problem 9.1.1, is there evidence of an association between infant birth weight and maternal age? Present results that support your conclusion.

9.1.3 What is the interpretation of $\widehat{\beta}_2$?

9.1.4 For a fixed effects analysis of these data, fit the following fixed effects model with linear trend for maternal age:

$$Y_{ij} = \beta_1 + \beta_2^{(FE)} \text{Age}_{ij} + \alpha_i + \epsilon_{ij},$$

where the α_i are considered fixed, not random effects, and $\epsilon_{ij} \sim N(0, \sigma_\epsilon^2)$.

9.1.5 From the results of the analysis for Problem 9.1.4, is there evidence of an association between infant birth weight and maternal age? Present results that support your conclusion.

9.1.6 What is the interpretation of $\widehat{\beta}_2^{(FE)}$?

9.1.7 Compare and contrast $\widehat{\beta}_2$ from the mixed effects model in Problem 9.1.1 and $\widehat{\beta}_2^{(FE)}$ from the fixed effects model in Problem 9.1.4. Explain why they might differ.

9.1.8 Consider a mixed effects model analysis of these data that allows for separate estimation of the cross-sectional and longitudinal effects of maternal age on infant birth weight. Fit the following mixed effects model with separate linear trends for the *cross-sectional* (C) and *longitudinal* (L) effects of maternal age:

$$Y_{ij} = \beta_1 + \beta_2^{(C)} \overline{\text{Age}}_i + \beta_2^{(L)} (\text{Age}_{ij} - \overline{\text{Age}}_i) + b_i + \epsilon_{ij},$$

where $b_i \sim N(0, \sigma_b^2)$ and $\epsilon_{ij} \sim N(0, \sigma_\epsilon^2)$.

9.1.9 What is the interpretation of $\widehat{\beta}_2^{(C)}$?

9.1.10 What is the interpretation of $\widehat{\beta}_2^{(L)}$?

9.1.11 Compare and contrast $\widehat{\beta}_2^{(C)}$ and $\widehat{\beta}_2^{(L)}$. Explain why they might differ.

9.1.12 Construct a formal test of H_0: $\beta_2^{(C)} = \beta_2^{(L)}$; this test can be based either on a Wald test or a likelihood-ratio test formed by comparing nested models. What do you conclude?

9.1.13 Compare and contrast $\widehat{\beta}_2^{(C)}$ and $\widehat{\beta}_2^{(L)}$ with $\widehat{\beta}_2$ from the mixed effects model in Problem 9.1.1 and $\widehat{\beta}_2^{(FE)}$ from the fixed effects model in Problem 9.1.4.