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Analyzing Repeated Measures Data
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In this newsletter we will compare several approaches to analyze repeated measures data.

Often data are collected on several occasions on the same experimental unit (often referred to as subject). This is the case, where, for instance, a child's height is recorded at several specific time points. In other instances data are collected on the same experimental unit under different experimental conditions, such as different doses of a drug in a clinical trial. These types of designs require an analysis method that can account for two sources of response variability - within-subject variability, and between-subject variability. This is due to the fact that measurements collected repeatedly on a given experimental unit are usually more similar than measurements taken across different experimental units. That is to say, observations measured repeatedly on a given subject are correlated.

Here we present a data set from an experiment where a score representing time spent on a certain task was measured on four occasions for each subject. Twelve subjects were randomly assigned to two levels of tension – high and low. A subject represents an experimental unit, tension is referred to as a between subject effect, and occasion - a within-subject effect. The data set can be organized in two different ways. One way is to use one row of data per subject and four variables to record the four scores. This format is often referred to as the wide, or multivariate, format. Another way to organize the data is to use four rows of data per subject and only one variable to record the score and an additional variable to indicate the four occasions. This is often called the long, or univariate, format. Most statistical software packages can automatically restructure data sets from the wide format to the long format and vice versa. For more information regarding the long and wide format data sets the reader can refer to an earlier newsletter: http://www.cscu.cornell.edu/news/statnews/stnews38.pdf

Data sets in either format can be used to analyze data from repeated measures designs. However, there are significant differences in the analysis methods used with each data structure. Crucial to these differences is the method used to model the covariances among the repeated measures. Several covariance structures are available to model the dependence between the repeated measurements within an experimental unit (Fig.1). The simplest covariance structure, called *simple* (Fig. 1a), assumes that the repeated measurements within a subject are uncorrelated. Since repeated measurements within a subject are often correlated, a simple covariance structure is not appropriate for modeling such data. A *compound symmetric* (CS) covariance structure (Fig. 1b) assumes a constant non-zero covariance between repeated measurements within each subject (within-subject component, $\boldsymbol{\sigma}^2$), a constant response variance between different subjects (between-subject component, $\boldsymbol{\sigma}_s^2$), and zero covariance between observations taken on different subjects. The most unrestrictive covariance structure that can be modeled in the repeated measures design is the *unstructured* covariance type (Fig. 1c) with arbitrary variances and covariances. Many more types of covariances structure are available including various autoregressive structures.

$$(a)\quad \begin{array}{l} Occasion1 \\ Occasion2 \\ Occasion3 \\ Occasion4 \end{array} \begin{vmatrix} \boldsymbol{\sigma}^2 & \mathbf{0} & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \boldsymbol{\sigma}^2 & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \boldsymbol{\sigma}^2 & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & \mathbf{0} & \boldsymbol{\sigma}^2 \end{vmatrix}$$

$$(b)\quad \begin{array}{l} Occasion1 \\ Occasion2 \\ Occasion3 \\ Occasion4 \end{array} \begin{vmatrix} \boldsymbol{\sigma}_s^2 + \boldsymbol{\sigma}^2 & \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 \\ \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 + \boldsymbol{\sigma}^2 & \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 \\ \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 + \boldsymbol{\sigma}^2 & \boldsymbol{\sigma}_s^2 \\ \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 & \boldsymbol{\sigma}_s^2 + \boldsymbol{\sigma}^2 \end{vmatrix}$$

$$(c)\quad \begin{array}{l} Occasion1 \\ Occasion2 \\ Occasion3 \\ Occasion4 \end{array} \begin{vmatrix} \boldsymbol{\sigma}_{11}^2 & \boldsymbol{\sigma}_{12}^2 & \boldsymbol{\sigma}_{13}^2 & \boldsymbol{\sigma}_{14}^2 \\ \boldsymbol{\sigma}_{21}^2 & \boldsymbol{\sigma}_{22}^2 & \boldsymbol{\sigma}_{23}^2 & \boldsymbol{\sigma}_{24}^2 \\ \boldsymbol{\sigma}_{31}^2 & \boldsymbol{\sigma}_{32}^2 & \boldsymbol{\sigma}_{33}^2 & \boldsymbol{\sigma}_{34}^2 \\ \boldsymbol{\sigma}_{41}^2 & \boldsymbol{\sigma}_{42}^2 & \boldsymbol{\sigma}_{43}^2 & \boldsymbol{\sigma}_{44}^2 \end{vmatrix}$$

Figure 1. Some covariance structures: (a) Simple, (b) Compound Symmetry (CS), (c) Unstructured. Diagonal elements represent variances, off diagonal elements represent covariances.

When analyzing data in the wide format, both univariate and multivariate analysis of variance (MANOVA) methods are available and are often presented simultaneously in the same output. Univariate analysis methods using wide format data require variances of all pair-wise differences in repeated measurements to be equal - a constraint called a sphericity assumption. The sphericity assumption is less restrictive than the compound symmetry assumption so if the compound symmetry assumption is met then so is the sphericity assumption but the converse is not true. In addition, tests for sphericity have been shown to have low power for small sample sizes and may falsely indicate lack of sphericity when sample sizes are very large. When the assumption of sphericity is badly violated, the F-statistics and the associated p-values for the within-subject hypotheses have been shown to be inflated, leading to false rejections of the null hypotheses. In such instances either adjustment can be made to the univariate test degrees of freedom (such as the Greenhouse-Geisser or Huynh-Feldt corrections), or one should use the MANOVA results.

The MANOVA approach, using the data in wide format, takes advantage of a general modeling technique used to model several response variables simultaneously. In order to be flexible to accommodate various designs it assumes the most unrestrictive covariance structure between responses – namely an unstructured covariance (Fig. 1c). Although this will produce a good fit, estimating a separate covariance for each response pair is often unnecessary and simpler covariance structures might be more appropriate. Most commonly used statistical packages such as SPSS, SAS, STATA, R and JMP are capable of performing the repeated measure analysis using data in the wide format.

A univariate method is also used when analyzing the data in the long format but sphericity is no longer a requirement for these types of models. An advantage of this method is the ability to model several types of covariance structures on repeated measurements. Choice of a specific covariance structure for the model will depend on the experimental design. Tests such as likelihood ratio tests are available to assess which covariance type fits the data best. This method can be implemented using mixed model procedures that are now available in the most commonly used statistical packages.

Besides allowing more flexibility in modeling the covariances between the repeated observations, the analysis using the long format has the additional advantage of being more flexible to incorporate covariates in the model. Still another advantage of the univariate approach with the data in the long format is the approach taken to handle missing data. Subjects that have some missing observations for one of the repeated measures will still be preserved in the analysis. In contrast, in analyzing data in wide format, subjects with even only one missing repeated measurement will be completely excluded from the analysis.

For further information regarding these various methods of analyzing repeated measure designs or if you would like some assistance in applying these in your research do not hesitate to contact the Cornell Statistical Consulting Unit.

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