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Multivariate Meta-Analysis as Structural Equation Models

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Abstract

Multivariate meta-analysis has become increasingly popular in the educational, social, and medical sciences. It is because the outcome measures in a meta-analysis may involve more than one effect size. This paper proposes two mathematically equivalent models to implement multivariate meta-analysis in structural equation modeling (SEM). Specifically, this paper shows how multivariate fixed-, random- and mixed-effects meta-analyses can be formulated as structural equation models. metaSEM (a free R package based on OpenMx) and Mplus are used to implement the proposed procedures. A real data set is used to illustrate the procedures. Formulating multivariate meta-analysis as structural equation models provides many new research opportunities for methodological development in both meta-analysis and SEM. Issues related to and extensions on the SEM-based meta-analysis are discussed.

Key words: multivariate meta-analysis, multivariate effect sizes, structural equation model, random-effects model, mixed-effects model

Multivariate Meta-analysis as Structural Equation Models

"Meta-analysis," a term coined by Glass (1976), is "the statistical analysis of a large collection of analysis results from individual studies for the purpose of integrating the findings" (p. 3). The first application of meta-analysis can be dated back to as early as 1904 by Karl Pearson (Chalmers, Hedges, & Cooper, 2002). After Glass' introduction to social sciences, meta-analysis has become a standard methodology to summarizing research findings in many disciplines. These disciplines include, but are not limited to, industrial and organizational psychology and management (Hunter & Schmidt, 2004), psychology (Cooper, 2010), education (Hedges & Olkin, 1985), public health (Mosteller & Colditz, 1996), epidemiology (Spitzer, 1995), clinical trials (Whitehead, 2002) and medical sciences (Sutton et al., 2000).

Many research questions are multivariate in nature. A single effect size may not be sufficient to summarize the outcome measures. Multiple effect sizes are generally required for such cases. Hence, many methodologists across various disciplines have developed methods to handle multivariate effect sizes in meta-analysis (e.g., Becker, 1992, 2000, 2009; Becker & Schram, 1994; Beretvas & Furlow, 2006; Berkey, Anderson, & Hoaglin, 1996; Berkey et al., 1998; Berrington & Cox, 2002; Cheung, 2010; Cheung & Chan, 2005, 2009; Furlow & Beretvas, 2005; Hafdahl, 2008; Kalaian & Raudenbush, 1996; Nam, Mengersen, & Garthwaite, 2003; Prevost et al., 2007; Raudenbush, Becker, & Kalaian, 1988; van Houwelingen, Arends, & Stijnen 2002).

There are several approaches to handle multivariate effect sizes (e.g., Cooper, 2010). One approach is to average the multivariate effect sizes within each study. Since

the averaged effect sizes are independent across studies, it is sufficient to apply univariate meta-analysis. This approach may work reasonably well in some settings. However, it is generally not appropriate when the multivariate effect sizes are measuring different constructs that should not be combined. For example, it may not make sense to average the gender differences (in terms of standardized mean difference) on motivation and on academic achievement. A second approach is to conduct univariate meta-analysis on each effect size separately. This approach looks appealing as it is easy to implement. However, it ignores the dependence among the effect sizes totally.

The third approach is to model the multivariate effect sizes simultaneously by taking the dependence among the effect sizes into account. Multivariate meta-analysis is usually more efficient than separate univariate meta-analysis because multivariate meta-analysis can "borrow strength" across the effect sizes (e.g., Berkey, Anderson, & Hoaglin, 1996; Riley, 2009; Riley et al., 2007a; Riley et al., 2007b; Ritz, Demidenko, & Spiegelman, 2008). It is because multivariate meta-analysis utilizes the correlation among the multivariate effects sizes. Many common multivariate effect sizes and their asymptotic sampling covariance matrices have been developed, for instance, the standardized mean differences with a common control group or multiple-endpoint with more than one effect sizes (Gleser & Olkin, 1994), correlation matrix (Becker, 1992), ordinal data (Bipat & Zwinderman, 2010), standard deviations (Raudenbush & Bryk, 2002), risk difference, risk ratio and odds ratio (Gleser & Olkin, 2009). This makes applying multivariate meta-analysis possible in many research domains.

Another popular statistical technique is structural equation modeling (SEM). It is a flexible statistical framework to model multivariate data in primary studies (e.g.,

Bollen, 1989). It has been extended to handle binary and categorical variables (Muthén, 1978), multilevel data (Bauer, 2003; Curran, 2002; Mehta & Neale, 2005; Skrondal & Rabe-Hesketh, 2004), mixture models (Lubke & Muthén, 2005; Muthén, 2008; Muthén & Asparouhov, 2009; Muthén & Shedden, 1999; Yung, 1997) and Bayesian analysis (Lee, 2007; Muthén & Asparouhov, in press). SEM is now a standard statistical model to fit various models in the social and behavioral sciences (Bollen, 2002; MacCallum & Austin, 2000; Tomarken & Waller, 2005).

Traditionally, SEM and meta-analysis are treated as two unrelated techniques in the literature. They have their own assumptions, models, notations, software packages and even journals (*Structural Equation Modeling: A Multidisciplinary Journal* and *Research Synthesis Methods*). Researchers familiar with one technique have to learn a new set of techniques in order to apply the other technique. Advances in one area have limited influence on the other area. This may limit the potential development in both areas.

Recently, Cheung (2008) proposed a model to integrate univariate meta-analysis into the SEM framework. His approach can be used to analyze univariate fixed-, random-, and mixed-effects meta-analysis as structural equation models. The primary objective of this paper is to extend Cheung's (2008) approach by showing how multivariate meta-analysis can be formulated as structural equation models. In addition, this paper also illustrates how to implement these procedures in a free R package called metaSEM (Cheung, 2011a) and Mplus (Muthén & Muthén, 2010). For the sake of discussion, this new approach is called *SEM-based meta-analysis* in this paper. Another objective of this paper is to introduce multivariate meta-analysis to the SEM audiences. By showing the

similarities between meta-analysis and SEM, readers can extend their SEM knowledge to meta-analysis. SEM users may even conduct meta-analysis without leaving the SEM framework.

This paper is organized as follows. In the following section I review the multivariate fixed-, random-, and mixed- effects meta-analytic models. The SEM-based meta-analysis is then presented. An example is used to demonstrate how the SEM-based meta-analysis may be applied in a real data set. Finally, issues related to and extensions on the SEM-based meta-analysis are discussed.

Multivariate Meta-analytic Models

Generally speaking, there are two classes of models in meta-analysis. They are the fixed-effects models and random-effects models (e.g., Borenstein, et al., 2010). Fixed-effects models usually assume that the population effect sizes are the same across studies while random-effects models assume each study has its own study specific effect sizes (cf. Bonett, 2009 and Shuster, 2010 for a different perspective). Fixed-effects models are appropriate if studies included in a meta-analysis are the population of interest. That is, researchers are only interested in drawing conclusions on the included studies. If researchers want to generalize findings beyond the included studies, random- or mixed-effects models are more appropriate assuming that the studies are randomly sampled from the population of interest (Hedges & Vevea, 1998; Hunter & Schmidt, 2000; National Research Council, 1992; Raudenbush, 2009).

It is more convenient to represent multivariate effect sizes in matrix notation. Let p be the number of effect sizes per study involved in a multivariate meta-analysis and p_i^* be the number of the observed effect sizes in the ith study. When there is no missing

effect size, p_i^* is the same as *p*; otherwise, p_i^* is smaller than *p*. The model for the *i*th study is

$$\mathbf{y}_i = X_i\boldsymbol{\beta}_i + \mathbf{e}_i, \quad (1)$$

where $\mathbf{y}_i$ is the $p_i^* \times 1$ vector of the observed effect sizes, X_i is a design matrix with 0 and 1 selecting the observed effect sizes, and $\boldsymbol{\beta}_i$ is a vector of the study specific effect sizes and $\mathbf{e}_i$ is a vector of sampling error.

The effect sizes $\mathbf{y}_i$ can be the raw or standardized mean differences, correlation coefficient, Fisher's *z* transformed score, log odds ratio, etc (see e.g., Borenstein, 2009; Fleiss & Berlin, 2009). When all effect sizes are observed in the *i*th study, that is, $p_i^* = p$, X_i is a $p \times p$ identity matrix; otherwise, it is a $p_i^* \times p$ selection matrix by excluding the rows with the missing effect sizes. For example, if there are 3 effect sizes per study involved in a meta-analysis. Study 1 is complete without missing data while the third effect size is missing in Study 2, the design matrices are $X_1 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \\ 0 & 0 & 1 \end{bmatrix}$ and $X_2 = \begin{bmatrix} 1 & 0 & 0 \\ 0 & 1 & 0 \end{bmatrix}$. $\mathbf{e}_i$ is assumed to be multivariate normally distributed with a mean vector of zero and a known covariance matrix V_i, that is, $\mathbf{e}_i \sim N(\mathbf{0}, V_i)$. As the effect sizes are correlated within a study in a multivariate meta-analysis, the off-diagonals of V_i are usually non-zero. Gleser and Olkin (1994, 2009) provided formulas for the conditional sampling covariance matrices of common effect sizes.

Fixed-effects Models

The population effect sizes are assumed the same under a fixed-effects model. The model for the stacked effect sizes of all studies is,

$$\mathbf{y} = X\boldsymbol{\beta}_{\text{fixed}} + \mathbf{e}, \tag{2}$$

where $\mathbf{y} = \left[\mathbf{y}_1^{\mathrm{T}} \,|\, \mathbf{y}_2^{\mathrm{T}} \,|\ldots|\, \mathbf{y}_k^{\mathrm{T}}\right]^{\mathrm{T}}$, $X = \left[X_1^{\mathrm{T}} \,|\, X_2^{\mathrm{T}} \,|\ldots|\, X_k^{\mathrm{T}}\right]^{\mathrm{T}}$ and $\mathbf{e} = \left[\mathbf{e}_1^{\mathrm{T}} \,|\, \mathbf{e}_2^{\mathrm{T}} \,|\ldots|\, \mathbf{e}_k^{\mathrm{T}}\right]^{\mathrm{T}}$. Becker (1992; see also Hedges & Olkin, 1985) provided a generalized least squares (GLS) approach to estimate $\boldsymbol{\beta}_{\text{fixed}}$,

$$\hat{\boldsymbol{\beta}}_{\text{fixed}} = (X^{\mathrm{T}}V^{-1}X)^{-1}X^{\mathrm{T}}V^{-1}\mathbf{y} \tag{3}$$

where $V = \text{Diag}\left[V_1, V_2, \ldots, V_k\right]$ is the conditional sampling covariance matrix of the effect sizes. Since the sampling covariance matrix is assumed known rather than estimated from the data, meta-analysis is also known as V-known models in the multilevel modeling literature (Hox 2010; Raudenbush & Bryk, 2002). The estimated asymptotic covariance matrix for $\hat{\boldsymbol{\beta}}_{\text{fixed}}$ is

$$\hat{\Omega}_{\text{fixed}} = (X^{\mathrm{T}}V^{-1}X)^{-1}. \tag{4}$$

The significance of the *i*th element in $\hat{\boldsymbol{\beta}}_{\text{fixed}}$ can be tested by a *Z* statistic. Under the null hypothesis $H_0 : (\boldsymbol{\beta}_{\text{fixed}})_i = 0$, the Z statistic,

$$Z = (\hat{\boldsymbol{\beta}}_{\text{fixed}})_i \,/\, \sqrt{(\hat{\Omega}_{\text{fixed}})_{ii}}, \tag{5}$$

where $(\hat{\Omega}_{\text{fixed}})_{ii}$ is the sampling variance of $(\hat{\boldsymbol{\beta}}_{\text{fixed}})_i$, is approximately normally distributed. Approximate confidence intervals (CIs) may also be constructed on $(\hat{\boldsymbol{\beta}}_{\text{fixed}})_i$.

To test the homogeneity of all effect sizes across the *k* studies, a *Q* statistic which is defined as:

$$Q = (\mathbf{y} - X\hat{\boldsymbol{\beta}}_{\text{fixed}})^{\mathrm{T}}V^{-1}(\mathbf{y} - X\hat{\boldsymbol{\beta}}_{\text{fixed}}) \tag{6}$$

is approximately distributed as a chi-square distribution with $\left(\sum_{i=1}^{k} p_i^* - p\right)$ degrees of freedom (*df*s) in large samples (see Becker, 1992; Demidenko, 2004; Hedges & Olkin, 1985). The above model can be easily extended to studies with covariates by using an appropriate design matrix in Equation 2 (see the following section under the mixed-effects models).

Random- and mixed-effects Models

Besides the sampling error, random-effects models include variations in the study specific effect sizes. The random-effect model for a multivariate meta-analysis is

$$\mathbf{y} = X\boldsymbol{\beta}_{\text{random}} + Z\mathbf{u} + \mathbf{e}, \qquad (7)$$

where $\mathbf{y}$, X and $\mathbf{e}$ are defined similarly as those in Equation 2, $\boldsymbol{\beta}_{\text{random}}$ is the mean population effect sizes under the random-effects model, $Z\mathbf{u} = \left[(Z_1\mathbf{u}_1)^{\mathrm{T}} \,|\, (Z_2\mathbf{u}_2)^{\mathrm{T}} \,|\, \ldots \,|\, (Z_k\mathbf{u}_k)^{\mathrm{T}}\right]^{\mathrm{T}}$ is the study specific effect with Z_i as a selection matrix of 1 and 0 selecting the appropriate study specific effect in the *i*th study. $\mathbf{u}_i \sim N(\mathbf{0}, T^2)$ is the study specific random effect in the *i*th study where T^2 is a $p \times p$ non-negative definite matrix.

In fixed-effects models, there is only one source of variation, the conditional sampling covariance matrix V_i. Besides the conditional sampling covariance matrix, random-effects models include an extra between-study variance component T^2. When $T^2 = 0$, the model is equivalent to a fixed-effects model.

The model in Equation 7 can be extended to include covariates by using a new design matrix that contains the study characteristics. For example, if there is a covariate

(e.g., duration of intervention in clinical studies) with the values of x_1 and x_2 for Studies 1 and 2 in our previous example, the design matrices would become

$X_1 = \begin{bmatrix} 1 & 0 & 0 & x_1 & 0 & 0 \\ 0 & 1 & 0 & 0 & x_1 & 0 \\ 0 & 0 & 1 & 0 & 0 & x_1 \end{bmatrix}$ and $X_2 = \begin{bmatrix} 1 & 0 & 0 & x_2 & 0 & 0 \\ 0 & 1 & 0 & 0 & x_2 & 0 \end{bmatrix}$. The values of the covariate are usually equal within the same study. However, they can be different sometimes.

Several procedures have been proposed to estimate the variance component T^2. Becker (1992), Demidenko (2004), and Jackson, White, and Thompson (2010) used method of moment while Becker and Schram (1994) applied an EM algorithm. Berkey et al. (1998) proposed an iterative procedure to estimate the variance component while Nam, Mengersen, and Garthwaite (2003) applied a Bayesian approach. Arends, Vokó, and Stijnen (2003), Kalaian and Raudenbush (1996), Raudenbush and Bryk (2002) and Stram (1996) used restricted maximum likelihood (REML) implemented inside a multilevel modeling approach to conduct multivariate meta-analysis. Prevost et al. (2007) empirically compared results based on some of these methods. However, limited simulation studies have been conducted to evaluate the empirical performance of these approaches in multivariate meta-analysis (but see Viechtbauer, 2005 for some empirical comparisons in univariate meta-analysis). Under the SEM-based meta-analysis, ML (and REML) may be used to estimate the variance component. Issues related to the estimation methods in estimating the variance components will be discussed later.

When $\hat{T}^2$ is computed, the estimate of $\boldsymbol{\beta}_{\text{random}}$ via GLS is

$$\hat{\boldsymbol{\beta}}_{\text{random}} = (X^{\mathrm{T}}\tilde{V}^{-1}X)^{-1}X^{\mathrm{T}}\tilde{V}^{-1}\mathbf{y} \qquad (8)$$

where $\widetilde{V} = \text{Diag}\left[\widetilde{V}_1, \widetilde{V}_2, \ldots, \widetilde{V}_k\right]$ is the unconditional sampling covariance matrix of the effect sizes with $\widetilde{V}_i = (Z_i \hat{T}^2 Z_i^{\mathrm{T}} + V_i)$. In the meta-analysis literature, V_i and $\widetilde{V}_i$ are known as the conditional and the unconditional sampling covariance matrices, respectively. The estimated asymptotic covariance matrix for $\hat{\boldsymbol{\beta}}_{\text{random}}$ is

$$\hat{\Omega}_{\text{random}} = (X^{\mathrm{T}} \widetilde{V}^{-1} X)^{-1}. \qquad (9)$$

Significances test and CIs on the elements of $\hat{\boldsymbol{\beta}}_{\text{random}}$ can be constructed similarly as in Equation 5.

Multivariate Meta-analyses as Structural Equation Models

One main difference between analyzing multivariate effect sizes in a meta-analysis and analyzing raw data in a structural equation model is that the multivariate effect sizes are distributed with known covariance matrices in meta-analysis. Cheung (2008) has a detailed account on how to handle this issue under a SEM framework for univariate meta-analysis. This paper proposes two mathematically equivalent approaches to handle multivariate effect sizes distributed with known covariance matrices in SEM. The first approach, based on the transformed effect sizes, is a direct extension of Cheung (2008). The second approach makes use of the full-information maximum likelihood (FIML) and definition variable (Mehta & Neale, 2005; Neale, 2000). In the following sections, I will introduce them one by one. The similarities and differences between them will then be discussed.

Structural Equation Models Based on the Transformed Effect Sizes

The distribution assumptions on the data are different in a meta-analysis and in a structural equation model. SEM usually assumes that data are independent and identically

distributed (cf. Mehta & Neale, 2005) while the effect sizes in a multivariate meta-analysis are distributed with known covariance matrices. Therefore, it is generally not appropriate to analyze effect sizes as raw data in SEM.

To make the multivariate effect sizes suitable for SEM, the effect sizes have to be transformed into such a way that they become independently and identically distributed (e.g., Kalaian & Raudenbush, 1996; Konstantopoulos, 2008; Kutner et al., 2005; Raudenbush, Becker, & Kalaian, 1988). Cheung (2008) applies this transformation on the univariate effect size. This paper extends it to multivariate effect sizes.

Fixed-effects meta-analysis. As shown in Equation 2, it is usually assumed that the population effect sizes $\boldsymbol{\beta}_{\text{fixed}}$ are the same under a fixed-effects model. First, we may calculate a transformation matrix $W^{1/2} = V^{-1/2}$ by taking the Cholesky decomposition on the inverse of V, the conditional sampling covariance matrix of the effect sizes. Applying Cholesky decomposition on a covariance matrix is similar to taking a square root on a variance. We pre-multiply the model in Equation 2 by $W^{1/2}$. The fixed-effects model becomes

$$W^{1/2}\mathbf{y} = W^{1/2}X\boldsymbol{\beta}_{\text{fixed}} + W^{1/2}\mathbf{e}, \tag{10}$$

$$\mathbf{y}^{*} = X^{*}\boldsymbol{\beta}_{\text{fixed}} + \mathbf{e}^{*},$$

where $\mathbf{y}^{*} = W^{1/2}\mathbf{y}$, $X^{*} = W^{1/2}X$, and $\mathbf{e}^{*} = W^{1/2}\mathbf{e}$. It can be readily shown that $\mathbf{e}^{*}$ is now distributed with a known identity matrix by considering

$$\text{var}(\mathbf{e}^{*}) = W^{1/2}\,\text{var}(\mathbf{e})(W^{1/2})^{\text{T}} \tag{11}$$

$$= W^{1/2}V(W^{1/2})^{\text{T}} = I,$$

as $W = V^{-1}$.

Originally, $\mathbf{e}_i$ is distributed with V_i in the *i*th study in Equation 2. After the transformation, $\mathbf{e}_i^*$ is independently and identically distributed with a known variance of 1. More importantly, the transformed effect sizes are now independent. This means that the transformed effect sizes can be treated as independent. Another key feature of the transformation is that it does not change the parameter space of $\boldsymbol{\beta}_{\text{fixed}}$. As the transformed error in Equation 11 is independently and identically distributed with a known variance of 1, we may use SEM to conduct a fixed-effects multivariate meta-analysis.

To simplify the notation, I present models on two effect sizes per study but the extension to more than two effect sizes is straightforward. Conventional graphical notations are used. Squares, circles and triangles represent the observed variables, the latent variables, and the means, respectively. Figure 1 shows a fixed-effects meta-analysis with two effect sizes per study. x_1^* and x_2^* are the transformed indicators taken from the transformed design matrix X^*.

A few crucial points should be noted here. First, the transformed effect sizes are stacked together as a single y^* regardless of how many effect sizes there are. x_1^* and x_2^* are used to indicate which effect sizes they are representing. Second, the error variance of y^* is fixed at 1 meaning that the conditional sampling variance on the transformed effect sizes is exactly 1. This constraint ensures that the estimated standard errors (*SE*s) of the parameter estimates are correct (see Cheung, 2008 for a discussion). Third, the intercept of y^* is fixed at 0. It is because the intercepts (population effect sizes) are explicitly represented by x_1^* and x_2^* in the model. By using this setup, the estimated population

effect sizes under the fixed-effects model are now represented by the regression coefficients b_1 and b_2 in the figure.

It may be of interest to test the homogeneity of the effect sizes. In the above formulation, we fix the error variance of y^* at 1 because it allows us to obtain the correct *SE*s for the parameter estimates. The *Q* statistic in Equation 6 can be re-expressed as

$$\begin{aligned} Q &= (\mathbf{y} - X\hat{\boldsymbol{\beta}}_{\text{fixed}})^{\mathrm{T}} V^{-1} (\mathbf{y} - X\hat{\boldsymbol{\beta}}_{\text{fixed}}) \\ &= (\mathbf{y} - X\hat{\boldsymbol{\beta}}_{\text{fixed}})^{\mathrm{T}} W (\mathbf{y} - X\hat{\boldsymbol{\beta}}_{\text{fixed}}) \\ &= (\mathbf{y} - X\hat{\boldsymbol{\beta}}_{\text{fixed}})^{\mathrm{T}} (W^{1/2})^{\mathrm{T}} W^{1/2} (\mathbf{y} - X\hat{\boldsymbol{\beta}}_{\text{fixed}}) \\ &= (\mathbf{y}^* - X^*\hat{\boldsymbol{\beta}}_{\text{fixed}})^{\mathrm{T}} (\mathbf{y}^* - X^*\hat{\boldsymbol{\beta}}_{\text{fixed}}) . \end{aligned} \tag{12}$$

Thus, the homogeneity statistic is equivalent to $Q = N\hat{\sigma}^2_{e^*}$ where $\hat{\sigma}^2_{e^*}$ is the unconstrained error variance of y^* and $N = \sum_{i=1}^{k} p_i^*$ is the "sample size" in SEM. We may free the error variance of y^* and calculate the *Q* statistic easily (see Appendix B for the Mplus code).

It should be noted that *N*, not *N*-1, is used in estimating $\hat{\sigma}^2_{e^*}$ because maximum likelihood (ML) estimation method is used in SEM. Moreover, the sample size (*N*) here is not equivalent to the number of studies in a meta-analysis. Since the effect sizes are stacked together, it is the number of studies times the number of effect sizes per study less the number of missing effect sizes.

Random- and mixed-effects meta-analysis. In Equation 10 we estimate $\boldsymbol{\beta}_{\text{fixed}}$ with the assumption that studies share common population effect sizes. To conduct a random- or a mixed-effects meta-analysis, we may introduce latent variables to represent the study specific effect sizes. The random-effects model with two effect sizes is

$$\mathbf{y}^* = \mathbf{x}_1^*.\mathbf{s}_1 + \mathbf{x}_2^*.\mathbf{s}_2 + \mathbf{e}^*, \quad (13)$$

where $\mathbf{y}^*$, $\mathbf{x}_1{}^*$, $\mathbf{x}_2{}^*$ and $\mathbf{e}^*$ are defined the same as those in the above equations. $\mathbf{s}_1$ and $\mathbf{s}_2$ are the $N \times 1$ latent variables representing the study specific effect sizes with $\begin{bmatrix} s_1 \\ s_2 \end{bmatrix} \sim N\left(\begin{bmatrix} \beta_1 \\ \beta_2 \end{bmatrix}, \begin{bmatrix} \tau_{11}^2 & \\ \tau_{21}^2 & \tau_{22}^2 \end{bmatrix} \right)$; and $\mathbf{x}_1^*.\mathbf{s}_1$ is the dot or elementwise product of $\mathbf{x}_1^*$ and $\mathbf{s}_1$. This model is known as the random slope analysis in Mplus which is similar to the random-coefficient model in multilevel modeling except that all equations are at the same level.

Figure 2 shows a random-effects meta-analysis with two effect sizes per study. s_1 and s_2 denote the latent variables (random slopes) that vary across subjects (the study specific effect sizes in the context of a meta-analysis). It should be noted that s_1 and s_2 are not parameters in the model because they are random variables. The means and the covariance matrix of these latent variables are the parameters that are actually estimated. β_1 and β_2 are the mean population effect sizes for $\boldsymbol{\beta}_{\text{random}}$ while $\begin{bmatrix} \tau_{11}^2 & \\ \tau_{21}^2 & \tau_{22}^2 \end{bmatrix}$ is the variance component T^2 in a multivariate random-effects meta-analysis.

To fit this model in SEM, we need to use random slope analysis. Mplus and Mx (Mehta & Neale, 2005; Muthén & Muthén, 2010; Neale, et al., 2006) may be used to conduct the analysis. It should be noted that both $\hat{\boldsymbol{\beta}}_{\text{random}}$ and the variance component $\hat{T}^2$ are estimated in a single step via the ML estimation method. This stands in contrast to the GLS approach in which the variance component T is estimated first and then the $\boldsymbol{\beta}_{\text{random}}$.

From the above models, it is clear that the same matrix $W^{1/2}$ is applied to both fixed-, random-, and mixed-effects models. It is because the objective of the transformation is to transform the conditional sampling variance of the error into an independent and identical distribution with a known variable of 1.

The random-effects model can be extended to a mixed-effects model with covariates. Suppose that there is a study characteristic *z*, the mixed-effects model becomes

$$\mathbf{y}^* = \mathbf{x}_1^*.\mathbf{s}_1 + \mathbf{x}_2^*.\mathbf{s}_2 + \mathbf{e}^*, \quad (14)$$

$$\mathbf{s}_1 = \beta_{11} + \beta_{12}\mathbf{z} + \mathbf{u}_1, \text{ and}$$

$$\mathbf{s}_2 = \beta_{21} + \beta_{22}\mathbf{z} + \mathbf{u}_2.$$

Figure 3 shows a mixed-effects model of two effect sizes per study with a covariate *z*. β_{11} and β_{12} are the intercept and regression coefficient on regressing the first effect size on *z* while β_{21} and β_{22} are the intercept and regression coefficient on regressing the second effect size on *z* and u_1 and u_2 are the study specific random effects (or residuals) with $\begin{bmatrix} u_1 \\ u_2 \end{bmatrix} \sim N\left(0, \begin{bmatrix} \tau_{11}^2 & \\ \tau_{21}^2 & \tau_{22}^2 \end{bmatrix}\right)$. u_1 and u_2 are now the residual heterogeneity matrix after controlling for *z*.

Structural Equation Models Based on the Definition Variables

The above parameterization involves extra transformation and the introduction of x_1^* and x_2^* is non-intuitive to many SEM users. It is because each study has its own sampling covariance matrices and most SEM packages cannot handle them properly. Thus, a transformation is required to make the transformed effect sizes distribute independently and identically. Besides the known sampling covariance matrices issue,

models and likelihood functions of the multivariate meta-analysis are indeed very simple. The log-likelihood function of a study in a random-effects meta-analysis is,

$$\log l(\boldsymbol{\beta}_{\text{random}}, T^2; \mathbf{y}_i) = \frac{-1}{2}\left\{p\log(2\pi) + \log\left|T^2 + V_i\right| + (\mathbf{y}_i - \boldsymbol{\beta}_{\text{random}})^{\mathrm{T}}(T^2 + V_i)^{-1}(\mathbf{y}_i - \boldsymbol{\beta}_{\text{random}})\right\}, \quad (15)$$

where p is the number of variables (or effect sizes; Demidenko, 2004; Hardy & Thompson, 1996).

The above log-likelihood function can be compared to a typical log-likelihood function in SEM with FIML as the estimation method (e.g., Arbuckle, 1996; Enders 2010),

$$\log l(\boldsymbol{\theta}; \mathbf{x}_i) = \frac{-1}{2}\left\{p\log(2\pi) + \log\left|\Sigma_i(\boldsymbol{\theta})\right| + (\mathbf{x}_i - \boldsymbol{\mu}_i(\boldsymbol{\theta}))^{\mathrm{T}}\Sigma_i(\boldsymbol{\theta})^{-1}(\mathbf{x}_i - \boldsymbol{\mu}_i(\boldsymbol{\theta}))\right\}, \quad (16)$$

where $\boldsymbol{\mu}_i(\boldsymbol{\theta})$ and $\Sigma_i(\boldsymbol{\theta})$ are the model implied mean vector and the model implied covariance matrix for the *i*th subject, respectively. By comparing these two log-likelihood functions, it becomes clear that we may analyze multivariate meta-analysis in SEM by setting $\boldsymbol{\mu}_i(\boldsymbol{\theta}) = \boldsymbol{\beta}_{\text{random}}$ and $\Sigma_i(\boldsymbol{\theta}) = T^2 + V_i$. The remaining issue is how to impose $(T^2 + V_i)$ that varies across subjects.

Currently some SEM packages such as OpenMx (Boker et al., 2011) and Mx (Neale et al., 2006) allow users to specify models with definition variables. Definition variables are observed variables that can be used to impose values on the parameters in a model. By using definition variables, the parameters or even the models can be different for different subjects. Neale (2000) used definition variables to illustrate moderated regression while Mehta and Neale (2005) used them to formulate multilevel SEM as a single level SEM. The key idea of analyzing multivariate effect sizes in SEM is to treat

each study in a multivariate meta-analysis as a subject in a structural equation model. Then definition variables are used to impose the known conditional sampling covariance matrices of each study.

Figure 4 shows a fixed-effects meta-analysis with two effect sizes. It is the same as the model listed in Equation 2. Since the sampling covariance matrix V_i of y_1 and y_2 are known in a meta-analysis, they are fixed via three definition variables. It should be noted that there is a subscript *i* in the figure emphasizing that V_i varies across subjects (or studies here in the context of meta-analysis). Moreover, y_1 and y_2 (not y_1^* and y_2^*) are directly used in the analysis. The model implied moments for the *i*th subject are $\boldsymbol{\mu}_i(\boldsymbol{\theta}) = \begin{bmatrix} b_1 \\ b_2 \end{bmatrix}$ and $\Sigma_i(\boldsymbol{\theta}) = V_i$. Now, b_1 and b_2 are the estimates of $\boldsymbol{\beta}_{\text{fixed}}$.

To fit a random-effects model, we have to include latent variables that representing the study specific random effects. Figure 5 shows a random-effects model with two effect sizes. It implements the model in Equation 7. The known conditional sampling covariance matrices are fixed via three definitions variables. The model implied moments for the *i*th subject are $\boldsymbol{\mu}_i(\boldsymbol{\theta}) = \begin{bmatrix} b_1 \\ b_2 \end{bmatrix}$ and $\Sigma_i(\boldsymbol{\theta}) = T^2 + V_i$. Two latent variables u_1 and u_2 with $\begin{bmatrix} u_1 \\ u_2 \end{bmatrix} \sim N\left(0, \begin{bmatrix} \tau_{11}^2 & \\ \tau_{21}^2 & \tau_{22}^2 \end{bmatrix}\right)$ represent the study specific random effects. The estimated covariance matrix between u_1 and u_2 is the estimated variance component $\hat{T}^2$ while b_1 and b_2 are the estimates of $\boldsymbol{\beta}_{\text{random}}$ under the random-effects model.

The above random-effects models can be easily extended to mixed-effects models by including study characteristics. Figure 6 shows a mixed-effects model with a study

characteristic *z*. The model implied moments for the effect sizes (excluding the predictor *z* for the ease of presentation) for the *i*th subject are simply $\boldsymbol{\mu}_i(\boldsymbol{\theta}) = \begin{bmatrix} b_{11} + b_{12} z_i \\ b_{21} + b_{22} z_i \end{bmatrix}$ and $\Sigma_i(\boldsymbol{\theta}) = \begin{bmatrix} b_{12}^2 & \\ b_{12} b_{22} & b_{22}^2 \end{bmatrix} \text{var}(z) + T^2 + V_i$. b_{12} and b_{22} represent the estimated regression coefficients from *z* to y_1 and y_2 while b_{11} and b_{21} represent the intercepts. $\hat{T}^2$ is the estimated residual heterogeneity matrix after controlling *z*.

Comparison between These Two Model Representations

Mathematically, the parameter spaces of these two model representations are the same. That is, the parameter estimates and their associated *SE*s are the same. These two models are similar to the case in regression analysis with weights – one can use weighted least squares directly or ordinary least squares on the transformed variables (Kutner et al., 2005). The results are equivalent for both models.

Since the effect sizes have to be transformed in the first approach, it is more tedious to implement it. There is another limitation in the first approach. The transformed effect sizes are stacked into a single variable as shown in the figures 1 to 3. The sample size in the SEM package is not the number of studies but the number of studies times the number of effect sizes less the number of incomplete effect sizes. In some SEM packages, e.g., Mplus, users may want to construct bootstrap CIs or conduct mixture modeling on the "subjects." When constructing a bootstrap CI, the transformed effect sizes (not the studies) will be resampled under this approach. It is not clear how this would affect the accuracy of the bootstrap CI. The same limitation applies to conducting mixture models on the multivariate effect sizes. Researchers should be cautious when

applying techniques such as bootstrap CI and mixture models in multivariate meta-analysis with the first approach.

Since no transformation is required for the approach using definition variables, it is more attractive. The limitation is that definition variables have only been implemented in OpenMx and Mx. Since many SEM users may not be familiar with the syntax of OpenMx or Mx, this may hinder applied users to fitting multivariate meta-analysis in SEM. To partially address this concern, a free R package called metaSEM (Cheung, 2011a) implemented in OpenMx and R (R Development Core Team, 2011) has been written. It uses simple commands to conduct univariate and multivariate meta-analysis (see the following illustrations). The following section will demonstrate how to conduct the SEM-based meta-analysis.

An Illustration with a Real Data Set

A data set from the World Values Survey II (World Values Study Group, 1994) was used to illustrate the procedures and analyses based on the SEM-based meta-analysis. Between 1990 and 1993, 57,561 adults aged 18 and above from 42 nations were interviewed by local academic institutes in Eastern European nations and by professional survey organizations in other nations.

Au and Cheung (2004) tested a theory on how job control predicts job satisfaction at the cultural level. Gross national product (GNP) was used as a control variable in their analyses. As an illustration, I extended Au and Cheung's theory to gender differences on life satisfaction and life control. Standardized mean difference (SMD) between males and females on life satisfaction ($SMD_{LifeSat}$) and on life control ($SMD_{LifeCon}$) were calculated in each country as the effect sizes. Positive values indicate that males have higher scores

than females do. GNP was used as a study characteristic in the mixed-effects meta-analysis. To improve the numerical stability of the results, GNP was centered and divided by 10,000 in the analyses. Table 1 shows the effect sizes, their associated sampling covariance matrices and the GNP.

The metaSEM package (Cheung, 2011a) and R (R Development Core Team, 2011) were used to perform the analyses. The R code was attached in Appendix A. Appendix B illustrates the steps to transform the effect sizes into independent and identical distribution. Mplus code for the same analysis based on transformed effect sizes was attached in Appendix C.[1] Since the results for the metaSEM package and Mplus were similar, only those based on the metaSEM package were reported. All of the results were reported to three decimal places.

A fixed-effect model was first fitted. The homogeneity test was statistically significant with $Q(df=82)=250.030$, $p<.001$. This suggests that the gender differences on life satisfaction and on life control vary across different cultural groups. A random-effects model was conducted. The pooled effect sizes were $\text{SMD}_{LifeSat} = 0.001$, $SE=0.014$, $p=.922$ and $\text{SMD}_{LifeCon} = 0.069$, $SE=0.017$, $p<.001$. The estimated variance component was $\hat{T} = \begin{bmatrix} 0.005 & \\ 0.004 & 0.008 \end{bmatrix}$. Figure 7 plots the pooled effect sizes, individual effect sizes and their 95% confidence ellipses. The small ellipse in solid line is the 95% confidence ellipse of the pooled effect sizes. It indicates the best estimate of the $\boldsymbol{\beta}_{\text{random}}$ in long run. The large ellipse in dashed line indicates where 95% of the study specific effects of studies may fall inside. In other words, it provides how the "true" population effect sizes of the studies vary.

As indicated by $\hat{T}$, the correlation between the population effect sizes was .624. This suggests that studies with higher $\text{SMD}_{LifeSat}$ tend to have higher $\text{SMD}_{LifeCon}$ as well.

To test the composite hypothesis $H_0 : \boldsymbol{\beta}_{\text{random}} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}$, I fitted a model by fixing both pooled effect sizes at 0. Since this model is nested within the model without constraint, a likelihood ratio (LR) test may be used to test the above composite hypothesis. The result was $\chi^2(df = 2) = 18.449, p < .001$ indicating that the pooled effect sizes are statistically different from zero. It is of interest to note that one pooled effect size $\text{SMD}_{LifeCon}$ is significant and the other one $\text{SMD}_{LifeSat}$ is non-significant while the multivariate test is significant. The multivariate test is usually more powerful than the individual univariate tests because the dependence between the two effect sizes has been taken into account.

A mixed-effects model with GNP as the covariate was then fitted. The regression coefficients and their *SE*s from GNP on $\text{SMD}_{LifeSat}$ and $\text{SMD}_{LifeCon}$ were $\hat{\beta}_{12} = -0.024$, *SE*=0.015, *p*=.116 and $\hat{\beta}_{22} = -0.037$, *SE*=0.018, *p*=.038, respectively. The estimated residual variance component was $\hat{T} = \begin{bmatrix} 0.005 & \\ 0.004 & 0.007 \end{bmatrix}$ after controlling GNP.

The results seem to suggest that the effect of GNP is stronger on $\text{SMD}_{LifeCon}$ than on $\text{SMD}_{LifeSat}$. We may verify this by testing the null hypothesis $H_0 : \beta_{12} = \beta_{22}$. Since a model with the equality constraint on the slopes is nested within a model without any constraint, a LR test may be used to compare them. The result was $\chi^2(df = 1) = 0.618, p = .432$ showing that we cannot reject the null hypothesis of equal regression coefficients. The pooled regression coefficient was -0.029, *SE*=0.014, *p*=.047.

Thus, further analysis shows that GNP was equally good at predicting both $SMD_{LifeSat}$ and $SMD_{LifeCon}$. Gender differences on life control and on life satisfaction are larger in countries with lower GNP.

Discussion and Future Directions

In this paper I showed how multivariate meta-analysis can be formulated as structural equation models. Two mathematically equivalent SEM models were proposed. The first approach is based on the transformed effect sizes. After the transformation, multivariate effect sizes can be treated as independent with a known sampling variance of 1. Some current SEM packages, e.g., Mplus, can be used to analyze the multivariate effect sizes properly.

The second approach is to analyze the multivariate effect sizes directly via FIML and definition variables. Each study in a meta-analysis is considered as a subject in SEM. The known sampling covariance matrices of each study are fixed via definition variables. The SEM-based meta-analysis allows researchers to easily test complicated models involving multivariate effect sizes and study characteristics.

Besides demonstrating how to conduct the SEM-based meta-analysis, the illustrations also highlight some advantages of the SEM-based meta-analysis. As the SEM-based meta-analysis is a structural equation model, equality and inequality constraints on the parameters can be easily imposed and tested (see Appendices A and C for the examples). Many interesting research hypotheses can be tested by formulating them as nested models. LR statistic can be used to compare them. In the following sections, I discuss some issues related to and further extensions on the SEM-based meta-analysis.

Statistical and Software Issues Related to the SEM-based Meta-analysis

Formulating meta-analyses as structural equation models is still a novel application of SEM (Cheung, 2008, 2009a, 2010). Most SEM packages were not designed for meta-analysis. FIML and definition variables are required to implement the SEM-based meta-analysis properly. Moreover, Cholesky decomposition on the variance component may sometimes be required to ensure that the estimated variance component stays non-negative definite. If the SEM-based meta-analysis is proved to be attractive to SEM or meta-analysis users, it should not be difficult to implement FIML and definition variables in major SEM packages.

Another issue is the estimation method for the variance component. Methods of moments, ML and REML have been proposed in the literature. In the context of meta-analysis, REML is usually preferred to ML in the family of maximum likelihood. It is because the estimated variance component based on REML is less biased than that on ML. In the SEM literature, ML is the most popular estimation method. REML is rarely used in SEM.

This paper only demonstrated analyses based on ML. The metaSEM package has also implemented the REML estimation method for both univariate and multivariate meta-analysis (Cheung, 2011b). One cautionary note is needed, however. Since the fixed-effects parameters have been removed before estimating the variance component with REML, the estimates do not include the fixed-effects. Therefore, one more step is required to estimate the fixed-effects parameters when REML is used as the estimation method. Moreover, model comparison with REML estimation method is only valid for the variance components.

Extensions to the SEM-based Meta-analysis

Cheung (2008) suggests several benefits of integrating meta-analysis into the SEM framework. One main advantage is that researchers can apply many state-of-the-art computational and modeling techniques implemented in the SEM packages. For example, likelihood-based CIs are often preferred to Wald CIs (Cheung, 2009b; Neale & Miller, 1997). This issue becomes more crucial when assessing the precision on the estimated variance components since the variance components are not normally distributed (Hardy & Thompson, 1996). The metaSEM package has also implemented the likelihood-based CIs on the fixed- and random-effects (see Cheung, 2011a for the examples).

As succinctly put by Shadish (1992, 1996; Shadish & Sweeney, 1991), many researchers are interested in the process of explaining variation of the effect sizes. Mediation and moderation models on the effect sizes may provide insights that cannot be gained in primary studies. Cook et al. (1992) also discussed issues and guidelines on formulating "causal" models in meta-analysis. By integrating meta-analysis into the SEM framework, mediation and moderation models on the effect sizes can be easily tested with structural equation models (e.g., Cheung, 2009a). This is another attractive feature of the SEM-based meta-analysis.

Another potential extension is Bayesian statistics. Bayesian inferences are becoming popular in meta-analysis especially when the number of studies is small (e.g., Sutton & Higgins, 2008). One obstacle of applying Bayesian meta-analysis is the lack of user friendly software. On the other side, Bayesian inferences are also getting more and more attention in SEM (Lee, 2007). The recent version of Mplus has implemented Bayesian inferences (Muthén & Asparouhov, in press). By formulating multivariate

meta-analyses as structural equation models, applied users may conduct Bayesian meta-analysis easily.

The popularity of SEM is partially due to its ability to integrate many existing techniques into a unified framework. Nowadays, SEM is a generic term for many divergent techniques such as, factor analysis, item response theory, categorical data analysis, multilevel modeling, missing data techniques, mixture modeling, Bayesian statistics and some combinations of them. Many SEM packages, such as, Mplus (Muthén, & Muthén, 2010), GLLAMM (Skrondal & Rabe-Hesketh, 2004) and EQS (Bentler, 2004), have implemented many of these techniques into a single package. Formulating multivariate meta-analysis as structural equation models provides many new research opportunities for methodological development in both meta-analysis and SEM. It is hoped that a unified but simple model may be available to both meta-analysts and SEM researchers in the near future.

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Endnote

[1]The complete data sets, the Mplus code, and the output are available at http://courses.nus.edu.sg/course/psycwlm/internet/multivariateMA.zip.

Table 1

Effect Sizes and Their Sampling Covariance Matrices from World Values Survey II (World Values Study Group, 1994)

County	SMD on LS	SMD on LC	Var(LS)	Cov (LS, LC)	Var(LC)	GNP
Argentina	-0.0321	0.0576	0.0040	0.0014	0.0042	2370
Austria	0.0801	0.0089	0.0029	0.0009	0.0029	4900
Belarus	0.0420	0.0741	0.0040	0.0013	0.0040	3110
Belgium	0.0078	0.1280	0.0015	0.0004	0.0015	15540
Brazil	0.1481	0.1821	0.0023	0.0008	0.0023	2680
Britain	0.0200	0.0445	0.0027	0.0012	0.0027	16100
Bulgaria	0.0266	0.1691	0.0040	0.0019	0.0041	NA
Canada	-0.0567	-0.0843	0.0023	0.0012	0.0023	20470
Chile	0.0507	0.2257	0.0027	0.0010	0.0027	1940
China	0.0777	0.1099	0.0042	0.0019	0.0042	1640
Czech	-0.0336	0.1071	0.0043	0.0015	0.0043	3140
Denmark	0.0972	0.2155	0.0039	0.0012	0.0040	22080
E Germany	-0.0013	0.0212	0.0030	0.0015	0.0031	NA
Estonia	0.1013	0.1827	0.0041	0.0012	0.0042	3830
Finland	-0.1127	0.0097	0.0070	0.0018	0.0070	26040
France	-0.0376	-0.0305	0.0040	0.0018	0.0041	19490
Hungary	-0.0558	-0.0654	0.0040	0.0013	0.0041	2780
Iceland	-0.1700	0.0400	0.0057	0.0021	0.0057	NA
India	-0.0247	0.2174	0.0016	0.0006	0.0017	350
Ireland	-0.0560	0.0382	0.0040	0.0017	0.0040	9550
Italy	0.1340	0.2240	0.0020	0.0007	0.0021	16830
Japan	-0.1256	-0.0291	0.0041	0.0012	0.0045	25430
Latvia	0.0538	-0.0201	0.0049	0.0015	0.0051	3410
Lithuania	0.0033	0.0676	0.0041	0.0010	0.0041	1630
Mexico	-0.1400	-0.0098	0.0027	0.0012	0.0027	2490
N Ireland	0.0129	0.1607	0.0135	0.0046	0.0136	16100
Netherlands	0.0186	0.1918	0.0040	0.0007	0.0040	17320
Nigeria	-0.2408	0.0315	0.0042	0.0010	0.0042	290
Norway	-0.1402	-0.0942	0.0032	0.0010	0.0033	23120
Poland	0.0560	0.0459	0.0043	0.0017	0.0045	1690
Portugal	0.1722	0.1405	0.0034	0.0012	0.0035	370
Romania	0.1058	0.3139	0.0037	0.0014	0.0037	2250
Russia	-0.0067	0.1932	0.0021	0.0006	0.0022	3220
S Africa	-0.0190	-0.0500	0.0015	0.0007	0.0015	2530

Note. LS=life satisfaction. LC=life control. NA=Not Available. NA represents missing value.

Table 1 (continued)

County	SMD on LS	SMD on LC	Var(LS)	Cov (LS, LC)	Var(LC)	GNP
S Korea	0.0332	-0.0998	0.0033	0.0007	0.0033	NA
Slovenia	0.0920	0.1464	0.0039	0.0015	0.0042	NA
Spain	0.0937	0.0729	0.0010	0.0004	0.0010	11020
Sweden	-0.0706	-0.2025	0.0039	0.0015	0.0039	23660
Switzerland	-0.0309	0.0497	0.0029	0.0010	0.0029	32680
Turkey	-0.2199	0.0963	0.0039	0.0000	0.0039	19060
USA	0.0031	-0.0063	0.0022	0.0010	0.0022	21790
W Germany	0.0081	0.0775	0.0019	0.0010	0.0019	22320

Figure Captions

Figure 1. Structural equation model on the transformed effect sizes for a fixed-effects meta-analysis with two effect sizes per study.

Figure 2. Structural equation model on the transformed effect sizes for a random-effects meta-analysis with two effect sizes per study.

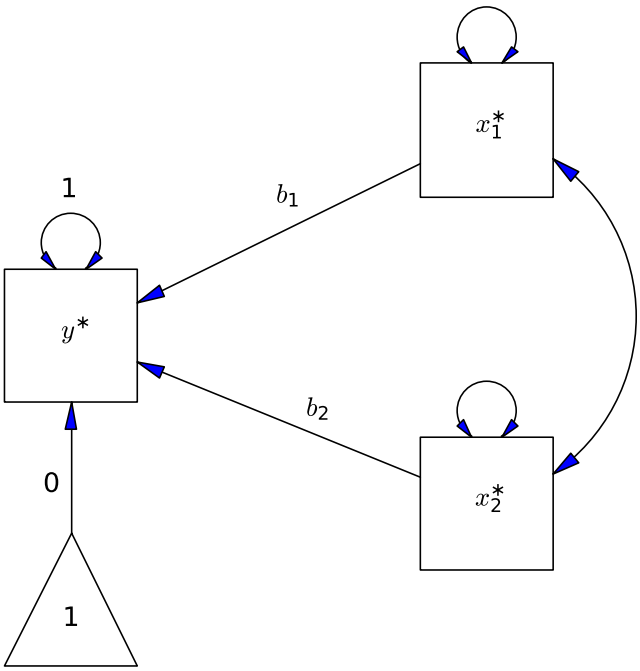
Figure 3. Structural equation model on the transformed effect sizes for a mixed-effects meta-analysis with two effect sizes and a covariate per study.

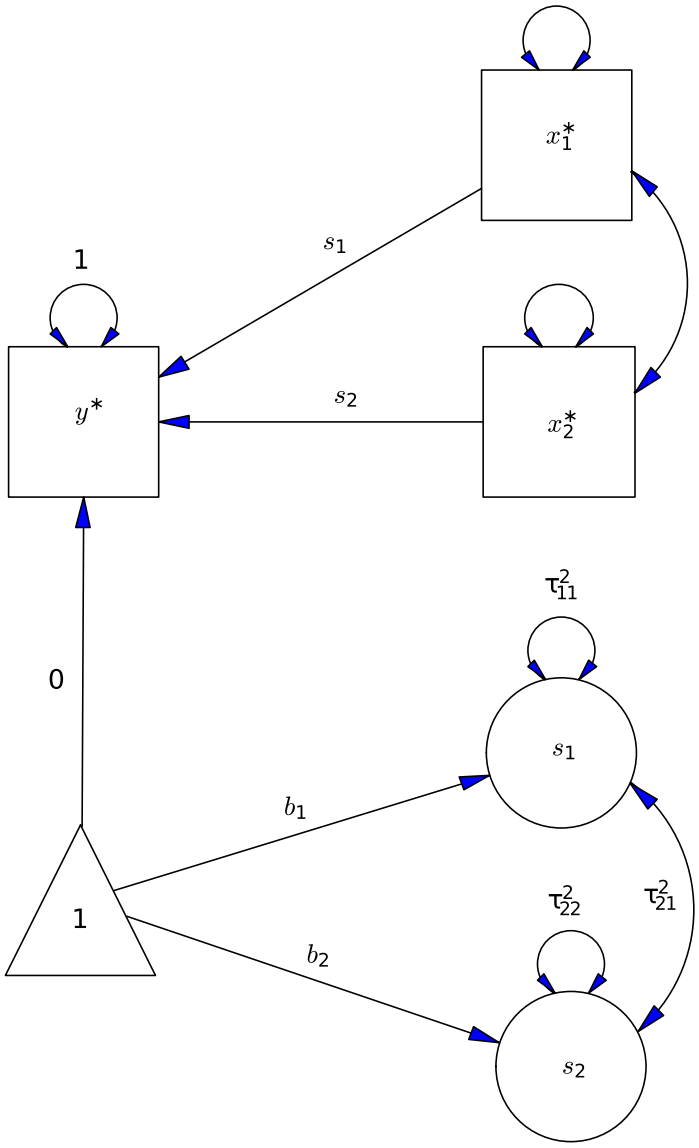
Figure 4. Structural equation model using the definition variables for a fixed-effects meta-analysis with two effect sizes per study.

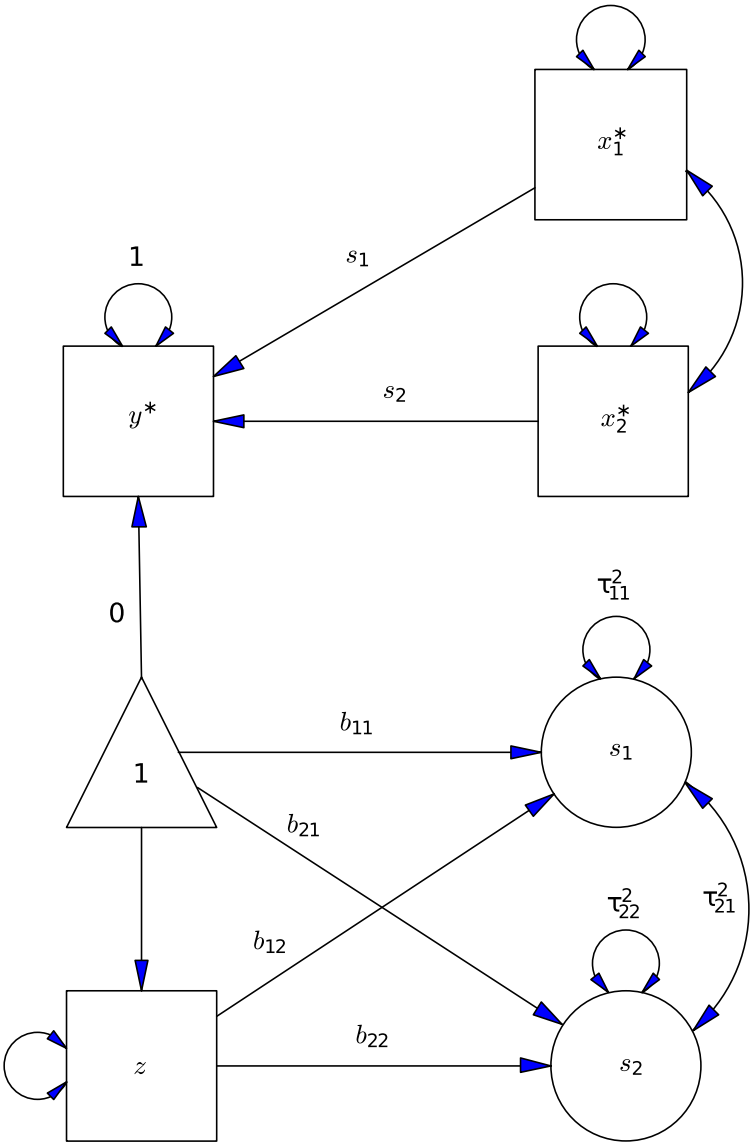
Figure 5. Structural equation model using the definition variables for a random-effects meta-analysis with two effect sizes per study.

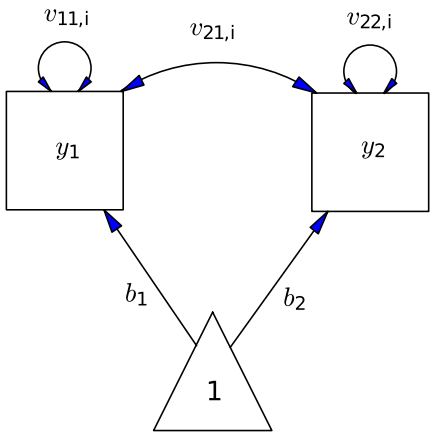
Figure 6. Structural equation model using the definition variables for a mixed-effects meta-analysis with two effect sizes and a covariate per study.

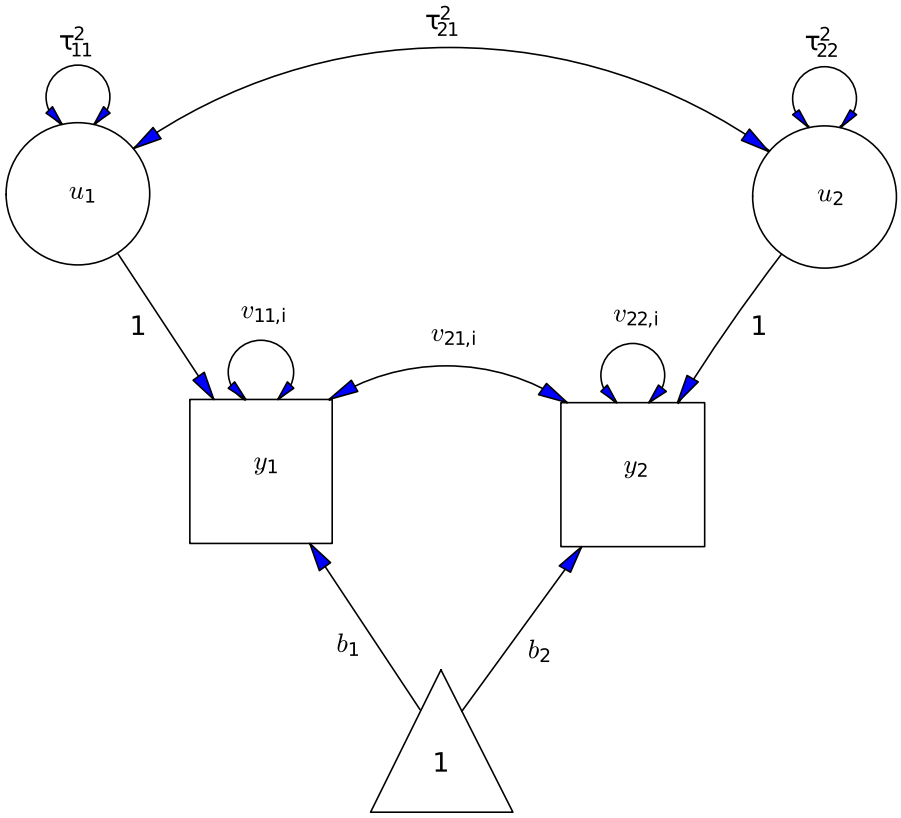
Figure 7. Plot of multivariate effect sizes and their 95% confidence ellipses.
The diamond in the centre is the estimated population effect sizes under a random-effects model. The solid ellipse (the closer one to the center) and the thick dash ellipse (the farther one to the center) around the estimated population effect sizes represent its 95% confidence ellipse and 95% confidence ellipse of the random effects, respectively. The diamonds in the horizontal and vertical axes represent the estimated effect sizes and their 95% confidence intervals. The arrows in the horizontal and vertical axes represent the 95% confidence intervals of the random effects.

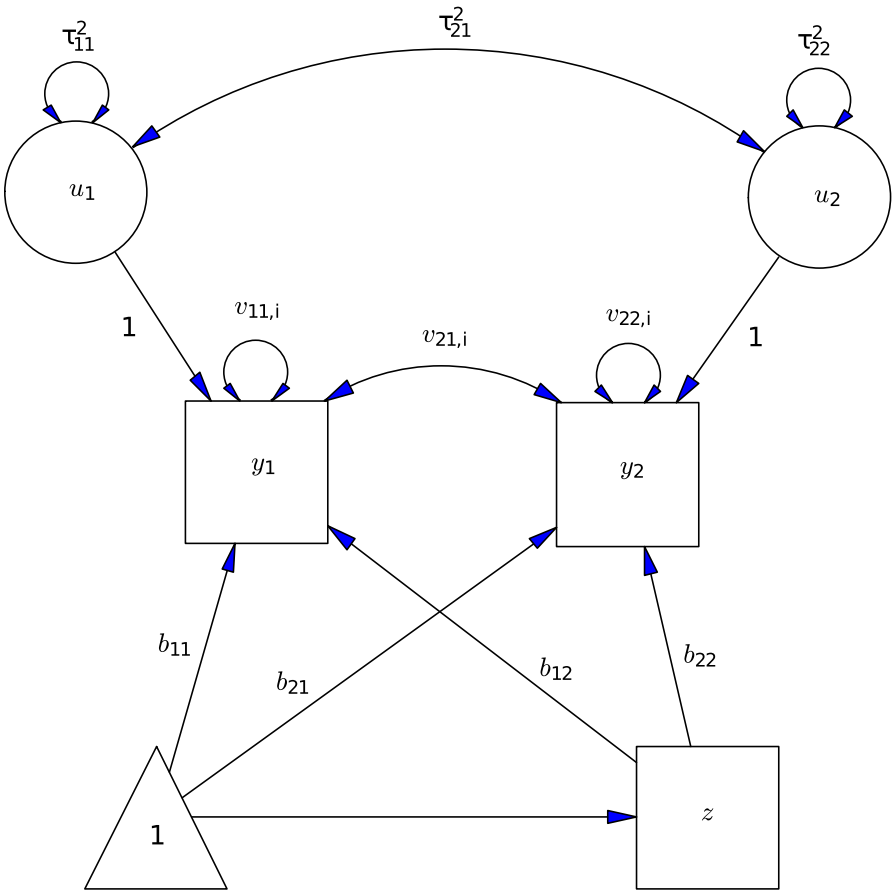

x_1^*
1
b_1
$y*$
b_2
x_2^*
0
1

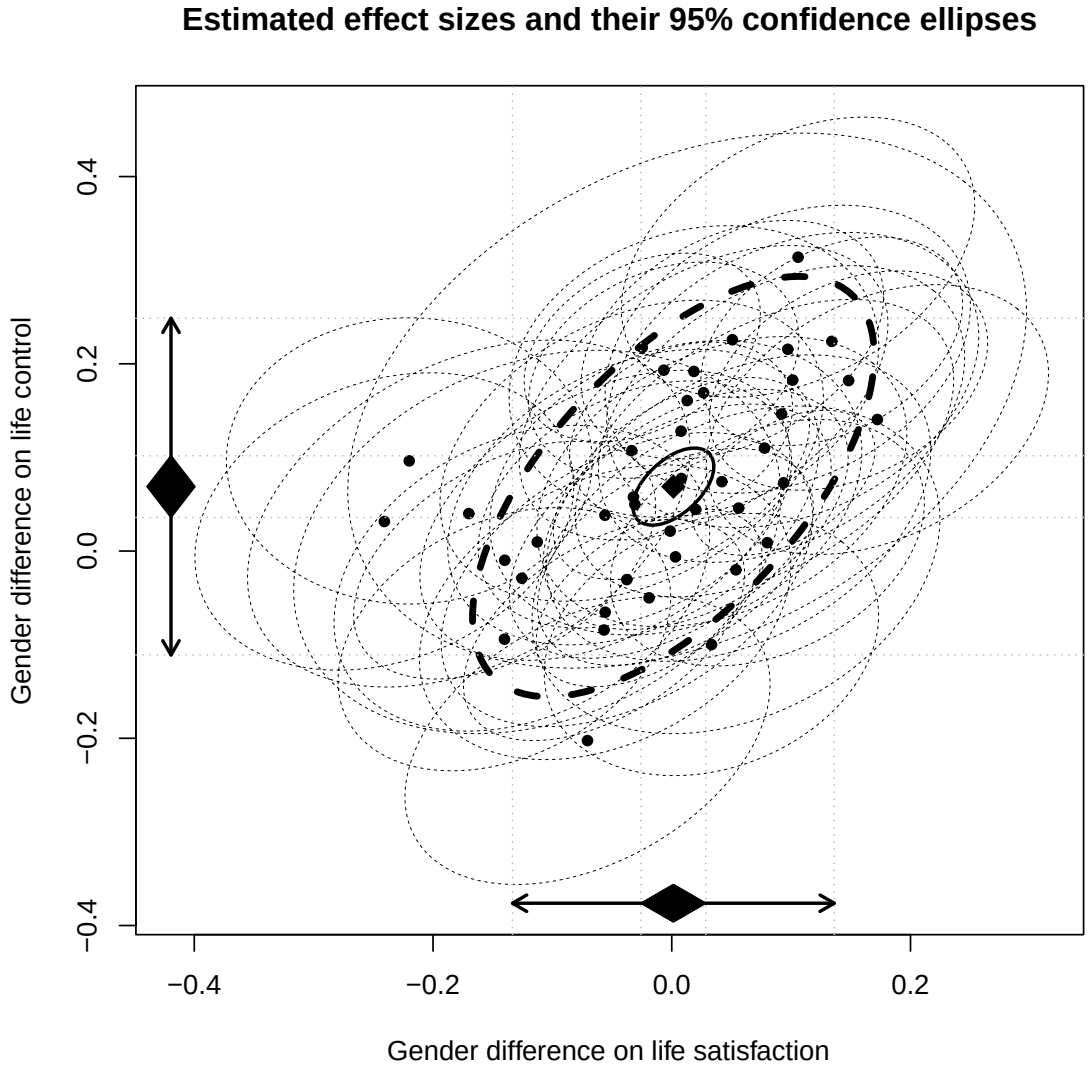

x_1^*
s_1
1
y^*
s_2
x_2^*
τ_{11}^2
0
s_1
b_1
1
τ_{22}^2
τ_{21}^2
b_2
s_2


x_1^*
1
s_1
y^*
s_2
x_2^*
0
τ_{11}^2
1
b_{11}
s_1
b_{21}
τ_{22}^2
τ_{21}^2
b_{12}
z
b_{22}
s_2


$v_{11,i}$
$v_{21,i}$
$v_{22,i}$
y_1
y_2
b_1
b_2
1


τ^2_{11}
τ^2_{21}
τ^2_{22}
u_1
u_2
1
$v_{11,i}$
$v_{21,i}$
$v_{22,i}$
1
y_1
y_2
b_1
b_2
1


τ^2_{11}
τ^2_{21}
τ^2_{22}
u_1
u_2
1
$v_{11,i}$
$v_{21,i}$
$v_{22,i}$
1
y_1
y_2
b_{11}
b_{21}
b_{12}
b_{22}
1
z


Estimated effect sizes and their 95% confidence ellipses
Gender difference on life control
Gender difference on life satisfaction
0.4
0.2
0.0
−0.2
−0.4
−0.4
−0.2
0.0
0.2

Appendix A

R Code for the Illustration

```
## Load the metaSEM library for the multivariate meta-analysis
## See http://courses.nus.edu.sg/course/psycwlm/internet/metaSEM/
library(metaSEM)

## Random-effects model.
## y: effect sizes;
## v: known sampling covariance matrices
random.ma1 <- meta(y=cbind(lifesat, lifecon), v=cbind(lifesat.var,
                   inter.cov, lifecon.var), data=wvs94,
                   model.name="Random effects model")
summary(random.ma1)

## Correlation between random effects
cov2cor(vec2symMat(coef(random.ma1, select=”random”)))

## Random-effects model.
## Test the null hypothesis of both population effect sizes are zero by
## intercept.constraints=matrix(0, nrow=1, ncol=2)
random.ma2 <- meta(y=cbind(lifesat, lifecon), v=cbind(lifesat.var,
                   inter.cov, lifecon.var), data=wvs94,
                   intercept.constraints=matrix(0, nrow=1, ncol=2),
                   model.name="Effect sizes are fixed at 0")
summary(random.ma2)

## Conduct a likelihood ratio test between these two models
anova(random.ma1, random.ma2)

## Fixed-effects model.
## Fix the variance component at 0 by using
## RE.constraints=matrix(0, ncol=2, nrow=2)
fixed.ma <- meta(y=cbind(lifesat, lifecon), v=cbind(lifesat.var,
                 inter.cov, lifecon.var), data=wvs94,
                 RE.constraints=matrix(0, ncol=2, nrow=2),
                 model.name="Fixed effects model")
summary(fixed.ma)

## Mixed-effects model.
## x: predictors
## gnp is divided by 10000 and centered by using
## scale(gnp/10000, scale=FALSE)
mixed.ma1 <- meta(y=cbind(lifesat, lifecon), v=cbind(lifesat.var,
                   inter.cov, lifecon.var),
                   x=scale(gnp/10000, scale=FALSE), data=wvs94,
                   model.name="GNP as a predictor")
summary(mixed.ma1)

## Mixed-effects model with equal regression coefficients.
## Fix the coefficients by using
## coef.constraints=matrix(c("0.0*Eq_slope", "0.0*Eq_slope"), nrow=2)
mixed.ma2 <- meta(y=cbind(lifesat, lifecon), v=cbind(lifesat.var,
                   inter.cov, lifecon.var),
                   x=scale(gnp/10000, scale=FALSE), data=wvs94,
```

```
                  coef.constraints=matrix(c("0.0*Eq_slope",
                                            "0.0*Eq_slope"), nrow=2),
                  model.name="GNP as a predictor with equal slope")
summary(mixed.ma2)

## Conduct a likelihood ratio test between these two models
anova(mixed.ma1, mixed.ma2)

## Plot the multivariate effect sizes
plot(random.ma1, study.min.cex=0.8, add.margin=0.02,
     estimate.ellipse.lwd=2, randeff.ellipse.lty=2,
     randeff.ellipse.lwd=4,
     main="Estimated effect sizes and their 95% confidence ellipses",
     axis.label=c("Gender difference on life satisfaction",
                  "Gender difference on life control"))
```

Appendix B

Example on Transforming the Effect Sizes into Independent and Identically Distributed

The following example illustrates the computations in preparing the data for the SEM-based meta-analysis on the transformed effect sizes. Suppose there are 3 studies with 2 effect sizes per study. Study 2 includes both effect sizes while Studies 1 and 3 have missing effect sizes in effect size 2 and effect size 1, respectively.

Let $\mathbf{y} = \begin{bmatrix} 0.3 \\ 0.4 \\ 0.5 \\ 0.6 \end{bmatrix}$, $X = \begin{bmatrix} 1 & 0 \\ 1 & 0 \\ 0 & 1 \\ 0 & 1 \end{bmatrix}$ and $V = \begin{bmatrix} 0.4 & 0 & 0 & 0 \\ 0 & 0.5 & 0.3 & 0 \\ 0 & 0.3 & 0.6 & 0 \\ 0 & 0 & 0 & 0.7 \end{bmatrix}$ be the data.

First, we calculate the transformation matrix $W^{1/2}$ based on the Cholesky decomposition $W^{1/2} = V^{-1/2} = \begin{bmatrix} 1.5811 & 0 & 0 & 0 \\ 0 & 1.6903 & -0.8452 & 0 \\ 0 & 0 & 1.2910 & 0 \\ 0 & 0 & 0 & 1.1952 \end{bmatrix}$. We pre-multiply $\mathbf{y}$ and X by $W^{1/2}$.

The data set in the SEM-based meta-analysis become $\mathbf{y}^* = W^{1/2}\mathbf{y} = \begin{bmatrix} 0.4743 \\ 0.2535 \\ 0.6455 \\ 0.7171 \end{bmatrix}$ and

$X^* = (W^{1/2}X) = \begin{bmatrix} 1.5811 & 0 \\ 1.6903 & -0.8452 \\ 0 & 1.2910 \\ 0 & 1.1952 \end{bmatrix}$. We may then export $\mathbf{y}^*$ and X^* for the SEM-based meta-analysis.

The following R code may be used to do the computations.

```
library(Matrix)   # Library used to create a block diagonal matrix
y <- matrix(c(0.3,0.4,0.5,0.6), ncol=1)   # Sample effect sizes
X <- matrix(c(1,1,0,0,0,0,1,1), ncol=2)   # Design matrix
# Sample asymptotic covariance matrix of effect sizes
V <- as.matrix(bdiag(0.4, matrix(c(0.5,0.3,0.3,0.6),ncol=2), 0.7))
W.5 <- chol(solve(V))                     # Transformation matrix
y.w <- W.5 %*% y                          # Transformed effect size
X.w <- W.5 %*% X                          # Transformed design matrix
y.w                                       # Display y.w

X.w                                       # Display X.w

wvs94 <- cbind(y.w, X.w)                  # Combine the data for output

write.table(wvs94, "wvs94.dat", sep="\t", na="*", row.names=FALSE,

            col.names=FALSE)              # Output for Mplus analysis
```

Appendix C

Mplus Code for the Illustration

```
TITLE:      Homogeneity test
DATA: FILE IS wvs94.dat;
VARIABLE: NAMES Study y InterLS InterLC GNP;
      USEVARIABLES ARE y InterLS InterLC;
      MISSING ARE *;
MODEL:
      y ON InterLS;
      y ON InterLC;
      [y@0.0];          ! Intercept of the effect size is fixed at 0.0
      y* (a);           ! Estimated error variance

MODEL CONSTRAINT:
      NEW(Q_stat);      ! Homogeneity statistic
      Q_stat = 84*a;    ! No. of effects * estimated error variance
OUTPUT: SAMPSTAT;
      CINTERVAL(symmetric);
```

```
TITLE:      Random-effects model
DATA: FILE IS wvs94.dat;
VARIABLE: NAMES Study y InterLS InterLC GNP;
      USEVARIABLES ARE y InterLS InterLC;
      MISSING ARE *;
ANALYSIS: TYPE=RANDOM;
      ESTIMATOR=ML;     ! Use ML method to calculate standard errors
MODEL:
      s_LS | y ON InterLS;
      s_LC | y ON InterLC;
      [y@0.0];          ! Intercept of the effect size is fixed at 0.0
      y@1.0             ! Error variance is fixed at 1.0
      s_LS*;            ! t1,1 in the figure
      s_LC*;            ! t2,1 in the figure
      s_LS WITH s_LC*;  ! t2,2 in the figure
      [s_LS*];          ! b1 in the figure
      [s_LC*];          ! b2 in the figure
OUTPUT: SAMPSTAT;
      CINTERVAL(symmetric);
```

```
TITLE:      Random-effects model: Fix population effect sizes at 0
DATA: FILE IS wvs94.dat;
VARIABLE: NAMES Study y InterLS InterLC GNP;
```

```
      USEVARIABLES ARE y InterLS InterLC;
      MISSING ARE *;
ANALYSIS: TYPE=RANDOM;
      ESTIMATOR=ML;     ! Use ML method to calculate standard errors
MODEL:
      s_LS | y ON InterLS;
      s_LC | y ON InterLC;
      [y@0.0];          ! Intercept of the effect size is fixed at 0.0
      y@1.0             ! Error variance is fixed at 1.0
      s_LS*;            ! t1,1 in the figure
      s_LC*;            ! t2,1 in the figure
      s_LS WITH s_LC*;  ! t2,2 in the figure
      [s_LS@0];         ! b1 fixed at 0
      [s_LC@0];         ! b2 fixed at 0
OUTPUT: SAMPSTAT;
      CINTERVAL(symmetric);
```

```
TITLE:      Mixed-effects model
DATA: FILE IS wvs94.dat;
VARIABLE: NAMES Study y InterLS InterLC GNP;
      USEVARIABLES ARE y InterLS InterLC GNP;
      MISSING ARE *;
      ! Centering is fine in this example as there is no missing data
      CENTERING IS GRANDMEAN(GNP);
      DEFINE: GNP=GNP/10000;
ANALYSIS: TYPE=RANDOM;
      ESTIMATOR=ML;     ! Use ML method to calculate standard errors
MODEL:
      s_LS | y ON InterLS;
      s_LC | y ON InterLC;
      [y@0.0];          ! Intercept of the effect size is fixed at 0.0
      y@1.0             ! Error variance is fixed at 1.0
      s_LS*;            ! t1,1 in the figure
      s_LC*;            ! t2,1 in the figure
      s_LS WITH s_LC*;  ! t2,2 in the figure
      [s_LS*];          ! b11 in the figure
      [s_LC*];          ! b21 in the figure
      s_LS ON GNP;      ! b12 in the figure
```

```
      s_LC ON GNP;      ! b22 in the figure
OUTPUT: SAMPSTAT;
      CINTERVAL(symmetric);
```

TITLE: Mixed-effects model with equality constraints on the slopes

```
DATA: FILE IS wvs94.dat;
VARIABLE: NAMES Study y InterLS InterLC GNP;
      USEVARIABLES ARE y InterLS InterLC GNP;
      MISSING ARE *;
      ! Centering is fine in this example as there is no missing data
      CENTERING IS GRANDMEAN(GNP);
      DEFINE: GNP=GNP/10000;
ANALYSIS: TYPE=RANDOM;
      ESTIMATOR=ML;     ! Use ML method to calculate standard errors
MODEL:
      s_LS | y ON InterLS;
      s_LC | y ON InterLC;
      [y@0.0];          ! Intercept of the effect size is fixed at 0.0
      y@1.0             ! Error variance is fixed at 1.0
      s_LS*;            ! t1,1 in the figure
      s_LC*;            ! t2,1 in the figure
      s_LS WITH s_LC*;  ! t2,2 in the figure
      [s_LS*];          ! b11 in the figure
      [s_LC*];          ! b21 in the figure
      s_LS ON GNP (1);  ! Regression coefficients are the same
      s_LC ON GNP (1);
OUTPUT: SAMPSTAT;
      CINTERVAL(symmetric);
```