metaSEM: An R Package for Meta-Analysis Using Structural Equation Modeling

Mike W.-L. Cheung
National University of Singapore

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Abstract

The **metaSEM** package provides functions to conducting univariate and multivariate meta-analysis using a structural equation modeling approach via the **OpenMx** package. It also implemented the two-stage structural equation modeling (TSSEM) approach to conducting fixed- and random-effects meta-analytic structural equation modeling (MASEM) on correlation/covariance matrices. This paper outlines the basic theories. Examples are used to illustrate the procedures.

Keywords:~meta-analysis, structural equation modeling, meta-analytic structural equation modeling, **metaSEM**, R.

1. Introduction

Meta-analysis is a popular technique to synthesizing research findings in social, behavioral, educational and medical sciences (Borenstein, Hedges, Higgins, and Rothstein 2009; Hedges and Olkin 1985; Hunter and Schmidt 2004; Whitehead 2002). There are several standalone packages for meta-analysis, e.g., Comprehensive Meta-Analysis and RevMan. Many standard statistical packages, for instance, SPSS (Lipsey and Wilson 2000), SAS (Arthur, Bennett, and Huffcutt 2001) and STATA (Sterne 2009), have macros or packages to fitting some meta-analytic models. Even in the R community, there are already several packages to conducting meta-analysis, for instance, **meta** (Schwarzer 2010), **rmeta** (Lumley 2009), **mvmeta** (Gasparrini 2012), **metaLik** (Guolo and Varin 2011) and **metafor** (Viechtbauer 2010).

The **metaSEM** package is yet another R package to conducting univariate and multivariate meta-analysis. It formulates meta-analytic models as structural equation models (Cheung 2008, 2011b) via the OpenMx package (Boker, Neale, Maes, Wilde, Spiegel, Brick, Spies, Estabrook, Kenny, Bates, Mehta, and Fox 2011). It also implemented the two-stage structural equation modeling (TSSEM) approach (Cheung and Chan 2005b, 2009) to conducting fixed- and random-effects meta-analytic structural equation modeling (MASEM) on correlation/covariance matrices. The main functions in this package are:

- `meta()` and `reml()`: `meta()` fits univariate and multivariate meta-analysis with maximum likelihood (ML) estimation method while `reml()` estimates the variance components of the random-effects with restricted (residual) maximum likelihood (REML) estimation method. Mixed-effects meta-analysis can be fitted by including study characteristics as predictors. Equality constraints on the intercepts, regression coefficients and variance components can be imposed.

- `meta3()` and `reml3()`: They fit 3-level meta-analysis by including clustering effect. `meta3()` fits the 3-level meta-analysis with ML estimation method while `reml3()` estimates the variance components with REML estimation method.
- `tssem1()`: It fits the first stage analysis of TSSEM by pooling correlation/covariance matrices with either a fixed- or random-effets model.
- `tssem2()`: It fits the second stage analysis of TSSEM by fitting structural models on the pooled correlation/covariance matrix. It is a wrapper of `wls()`.
- `wls()`: It fits a correlation/covariance structure analysis with weighted least squares (WLS) estimation method.

Besides reporting Wald confidence intervals (CIs) based on z statistic, likelihood-based CIs on the parameter estimates may also be requested (Cheung 2009a; Neale and Miller 1997). Several generic functions, such as `anova()`, `coef()`, `vcov()`, `print()`, `summary()` and `plot()`, have been implemented.

This paper was based on the **metaSEM** package version 0.7-1 and the **OpenMx** package version 1.2.4-2063. The paper is organized as follows. The next section presents basic ideas on structural equation models and how they are linked to meta-analytic models. Basic theory on the TSSEM are then presented. Several examples are used to illustrate these procedures.

2. Structural Equation Modeling Based Meta-Analysis

In this section, basic structural equation models are introduced. Univariate and multivariate meta-analysis are treated as special cases of SEM (Cheung 2008, 2011b).

2.1. Structural equation model

Structural equation modeling is a multivariate technique to fitting and testing hypothesized models. Let $\mathbf{y}$ be a $p \times 1$ vector of the sample data where p is the number of variables. It is hypothesized that the model for the first and second moments are $\mu = \mu(\theta)$ and $\mathbf{\Sigma} = \mathbf{\Sigma}(\theta)$, respectively, where θ is a vector of parameters.

The -2*log-likelihood of the ith case is:

$$-2 * logL_i(\theta; \mathbf{y}_i)_{\mathrm{ML}} = p_i * log(2\pi) + log|\mathbf{\Sigma_i}(\theta)| + (\mathbf{y}_i - \mu_{\mathbf{i}}(\theta))'\mathbf{\Sigma_i}(\theta)^{-1}(\mathbf{y}_i - \mu_{\mathbf{i}}(\theta)), \quad (1)$$

where p_i is the number of variables in the ith case, $\mu_{\mathbf{i}}(\theta)$ and $\mathbf{\Sigma_i}(\theta)$ are the model implied mean vector and the model implied covariance matrix for the ith case, respectively. Since there is a subscript i in these quantities, the model implied mean vector and covariance matrix may vary across cases. In order words, this model handles incomplete data automatically by selecting only the complete variables in the log-likelihood function.

To obtain the parameter estimates, we may take the sum of the -2*log-likelihood over all cases and minimize it. This is known as the full information maximum likelihood (FIML or simply

ML) estimation method. Iterative methods are usually used to obtain the solutions. If it is convergent, the asymptotic covariance matrix (thus the standard errors) of the parameter estimates may be obtained from the inverse of the Hessian matrix. The parameter estimates divided by their standard errors follow a z distribution under the null hypothesis. Moreover, likelihood ratio statistic may also be used to compare nested models.

2.2. Univariate fixed-effects model

When there is only one effect size, the univariate fixed-effects model for the ith study is:

$$y_i = \beta_{\text{fixed}} + e_i, \tag{2}$$

where β_{fixed} is the common effect under a fixed-effects model and $\text{var}(e_i) = v_i$ is the known sampling variance. To fit the unvariate fixed-effects meta-analysis in SEM, we may use the following model:

$$\mu_i(\theta) = \beta_{\text{fixed}} \tag{3}$$

and

$$\mathbf{\Sigma}_i(\theta) = v_i \tag{4}$$

Since v_i is known, the only parameter in the univariate fixed-effects model is β_{fixed} .

2.3. Univariate random-effects model

A random-effects model allows studies to have their own study specific effect. The model for the ith study is:

$$y_i = \beta_{\text{random}} + u_i + e_i. \tag{5}$$

where β_{random} is the average effect under a random-effects model and $\text{var}(u_i) = \tau^2$ is the heterogeneity variance that has to be estimated. To fit the unvariate fixed-effects meta-analysis in SEM, we may use the following model:

$$\mu_i(\theta) = \beta_{\text{random}} \tag{6}$$

and

$$\mathbf{\Sigma}_i(\theta) = \tau^2 + v_i \tag{7}$$

In this model we have to estimate both β_{random} and τ^2.

2.4. Univariate mixed-effects model

The mixed-effects meta-analysis extends the random-effects meta-analysis by including study characteristics as predictors. Assuming that $\mathbf{x}_i$ is a $m \times 1$ vector of predictors where m is the number predictors in the ith study, the model is:

$$y_i = \beta_0 + \beta'\mathbf{x}_i + u_i + e_i, \tag{8}$$

where β is a vector of regression coefficients.

To fit the univariate mixed-effects meta-analysis in SEM, we may use the following model for the conditional mean and variance:

$$\mu_i(\theta|\mathbf{x}_i) = \beta_0 + \beta'\mathbf{x}_i \tag{9}$$

and

$$\mathbf{\Sigma}_i(\theta|\mathbf{x}_i) = \tau^2 + v_i. \tag{10}$$

Since $\mathbf{x}_i$ is specified via definition variables (Boker et ˜al. 2011), the means and covariance matrix of $\mathbf{x}$ are not estimated. That is, $\mathbf{x}$ is treated as a design matrix rather than random variables.

2.5. Multivariate mixed-effects model

Let us assume that there are p effect sizes with m predictors in k studies. The model for the multivariate effect sizes in the ith study is:

$$\mathbf{y}_i = \mathbf{B}\mathbf{x}_i + \mathbf{u}_i + \mathbf{e}_i, \tag{11}$$

where $\mathbf{y}_i$ is a $p \times 1$ effect sizes, $\mathbf{B}$ is a $p \times (m+1)$ regression coefficients including the intercepts, $\mathbf{x}_i$ is a $(m+1) \times 1$ predictors including 1 in the first column, $\mathbf{u}_i$ is a $p \times 1$ study specific random effects, and $\mathbf{e}_i$ is a $p \times 1$ sampling error. We assume that $\mathrm{var}(\mathbf{e}_i) = V_i$ is known and given in the ith study and $\mathrm{var}(\mathbf{u}_i) = T^2$ is the variance component of the between-study heterogeneity that has to be estimated.

The -2*log-likelihood of the above model is:

$$-2 * logL_i(\mathbf{B}, T^2; \mathbf{y}_i)_{\mathrm{ML}} = p_i * log(2\pi) + log|T^2 + V_i| + (\mathbf{y}_i - \mathbf{B}\mathbf{x}_i)'(T^2 + V_i)^{-1}(\mathbf{y}_i - \mathbf{B}\mathbf{x}_i), \tag{12}$$

where p_i is the number of effect sizes in the ith study.

In applied research, different studies may report different effect sizes, that is, p_i may vary across studies. The above -2*log-likelihood may handle missing effect sizes by using different dimenions of the elements in the above equation. It is expected that there is no missing data in $\mathbf{x}_i$. When there are missing data in $\mathbf{x}_i$, the whole study will be deleted before the analysis.

2.6. Restricted Maximum Likelihood (REML) Estimation Method

Since both the fixed- and random-effects are estimated simultaneously, it is well-known that $\hat{T}^2_{\mathrm{ML}}$ based on the ML estimation is negatively biased. It is because it does not take the uncertainty in estimating $\hat{\mathbf{B}}_{\mathrm{ML}}$ into account. If the unbiasness of the variance component is crucial in the research questions, we may obtain the variance component $\hat{T}^2_{\mathrm{REML}}$ based on the REML estimation method (Cheung 2011a; Harville 1977; Patterson and Thompson 1971).

The -2log-likelihood of the model is:

$$-2logL_i(T^2; \mathbf{y}_i)_{\mathrm{REML}} = p_i * log(2\pi) + log|T^2 + V_i| + (\mathbf{y}_i - \alpha\mathbf{X}_i)'(T^2 + V_i)^{-1}(\mathbf{y}_i - \alpha\mathbf{X}_i) + |X_i' V_i^{-1} X_i|, \tag{13}$$

where $\alpha = (X'V^{-1}X)^{-1}X'V^{-1}\mathbf{y}$.

Since the fixed effects $\mathbf{B}$ is not involved in the above -2log-likelihood function, it has to be calculated in a second stage.

2.7. Three-level meta-analysis

Observed effect sizes may be related or dependent. For example, effect sizes reported by the same research team may be more similar when comparing to effect sizes reported by other research teams. Effect sizes reported by studies from the same country may be more similar when comparing to studies across countries. If the degree of dependence is known, multivariate meta-analysis as introduced before may be applied. When the degree of dependence is unknown, a three-level meta-analytic model may be used (Konstantopoulos 2011). The model is:

$$y_i = \beta_0 + \beta' \mathbf{x}_i + u_{(2)i} + u_{(3)i} + e_i, \tag{14}$$

where $u_{(2)i}$ and $u_{(3)i}$ are the random-effects at level-2 and level-3, respectively.

To fit the three-level meta-analytic model in SEM, we may use the following model for the conditional mean and variance:

$$\mu_i(\theta|\mathbf{x}_i) = \beta_0 + \beta' \mathbf{x}_i \tag{15}$$

and

$$\mathbf{\Sigma}_i(\theta|\mathbf{x}_i) = \tau^2_{(2)} + \tau^2_{(3)} + v_i. \tag{16}$$

where $\tau^2_{(2)} = \text{var}(u_{(2)i})$ and $\tau^2_{(3)} = \text{var}(u_{(3)i})$ are the heterogeneity at level-2 and level-3, respectively.

2.8. Examples

Two example data sets are used to demonstrate the procedures of fitting univariate and multivariate meta-analyses. The first data set was taken from Becker (1983) who reported 10 studies on sex differences in conformity using the fictitious norm group paradigm. *di* and *vi* are the standardized mean difference and its sampling variance, respectively. Becker hypothesized that the logarithm of the number of items (*items*) predicted the effect size.

The second data set is adapted from Berkey, Hoaglin, Antczak-Bouckoms, Mosteller, and Colditz (1998). They summarized five published trials comparing surgical and non-surgical treatments for medium-severity periodontal disease, one year after treatment. Publication year *pub_year* was hypothesized as a predictor.

Univariate random-effects model The function `meta()` is used to conduct the analyses. The arguments `y` and `v` are used to specify the effect sizes and its sampling variances (and covariances for multivariate meta-analysis), respectively. By default, a random-effects meta-analysis is fitted. After running the analysis, `summary()` is used to extract the results. The estimated fixed- and random-effects are represented by the **Intercept** and **Tau2** parameters. `coef()` and `vcov()` may be used to extract the parameter estimates and their asymptotic sampling covariance matrix, respectively.

From the following analyses, the Q statistic ($df = 9$) is 30.6495, $p < .001$ and the I^2 based on the Q statistic is .6718. The pooled effect size with its 95% Wald confidence interval (CI) based on the random-effects model is 0.1747 (-0.0475, 0.3970). The estimated heterogeneity variance is 0.0774.

```
R> ## Load the library
R> library(metaSEM)
R> ## Show the first few studies of the data set
R> head(Becker83)
```

```
  study    di   vi percentage items
1     1 -0.33 0.03         25     2
2     2  0.07 0.03         25     2
3     3 -0.30 0.02         50     2
4     4  0.35 0.02        100    38
5     5  0.69 0.07        100    30
6     6  0.81 0.22        100    45

R> ## Random-effects meta-analysis with ML
R> summary( random1 <- meta(y=di, v=vi, data=Becker83) )

Running Meta analysis with ML

Call:
meta(y = di, v = vi, data = Becker83)

95% confidence intervals: z statistic approximation
Coefficients:
            Estimate Std.Error    lbound    ubound z value
Intercept1  0.174734  0.113378 -0.047482  0.396950  1.5412
Tau2_1_1    0.077376  0.054108 -0.028674  0.183426  1.4300
           Pr(>|z|)
Intercept1   0.1233
Tau2_1_1     0.1527

Q statistic on homogeneity of effect sizes: 30.64949
Degrees of freedom of the Q statistic: 9
P value of the Q statistic: 0.0003399239
Heterogeneity indices (based on the estimated Tau2):
                             Estimate
Intercept1: I2 (Q statistic)   0.6718

Number of studies (or clusters): 10
Number of observed statistics: 10
Number of estimated parameters: 2
Degrees of freedom: 8
-2 log likelihood: 7.928307
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Exact the coefficients
R> coef(random1)

Intercept1   Tau2_1_1
0.17473402 0.07737594

R> ## Exact the sampling variance covariance matrix
R> vcov(random1)
```

```
            Intercept1    Tau2_1_1
Intercept1 0.012854471 0.001240975
Tau2_1_1   0.001240975 0.002927667
```

Univariate mixed-effects model We may include a predictor to conduct a mixed-effects meta-analysis. The argument `x` is used to specify the predictors. If there are more than one predictor, `cbind()` may be used to specify them. The estimated regression coefficients are represented by the **Slope** parameter. The following analysis suggests that $log(items)$ is a significant predictor with the estimated regression coefficient and its 95% CI of 0.2109 (0.1225, 2.9924) with $R^2 = 1$.

```
R> ## Mixed-effects meta-analysis with "log(items)" as the predictor
R> summary( mixed1 <- meta(y=di, v=vi, x=log(items), data=Becker83) )

Running Meta analysis with ML

Call:
meta(y = di, v = vi, x = log(items), data = Becker83)

95% confidence intervals: z statistic approximation
Coefficients:
              Estimate   Std.Error      lbound      ubound
Intercept1 -3.2015e-01  1.0981e-01 -5.3539e-01 -1.0492e-01
Slope1_1    2.1088e-01  4.5084e-02  1.2251e-01  2.9924e-01
Tau2_1_1    1.0000e-10  2.0095e-02 -3.9386e-02  3.9386e-02
           z value  Pr(>|z|)
Intercept1 -2.9154  0.003552 **
Slope1_1    4.6774 2.905e-06 ***
Tau2_1_1    0.0000  1.000000
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Q statistic on homogeneity of effect sizes: 30.64949
Degrees of freedom of the Q statistic: 9
P value of the Q statistic: 0.0003399239
Explained variances (R2):
                           Estimate
y1: Tau2 (no predictor)      0.0774
y1: Tau2 (with predictors)   0.0000
y1: R2                       1.0000

Number of studies (or clusters): 10
Number of observed statistics: 10
Number of estimated parameters: 3
Degrees of freedom: 7
-2 log likelihood: -4.208024
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

```
R> ## Exact the coefficients
R> coef(mixed1)

   Intercept1      Slope1_1      Tau2_1_1
-0.3201549197  0.2108782268  0.0000000001

R> ## Exact the sampling variance covariance matrix
R> vcov(mixed1)

              Intercept1      Slope1_1     Tau2_1_1
Intercept1  0.0120593278 -3.940014e-03 3.887682e-04
Slope1_1   -0.0039400143  2.032587e-03 8.408773e-05
Tau2_1_1    0.0003887682  8.408773e-05 4.038148e-04
```

Univariate fixed-effects model Mathematically, fixed-effects meta-analysis is a special case of the random-effects meta-analysis by fixing the variance of the random-effects at 0. The argument `RE.constraints`, which expects a matrix as input, is used to constrain the variance component of the random effects.

```
R> ## Fixed-effects meta-analysis
R> summary( fixed1 <- meta(y=di, v=vi, data=Becker83,
                          RE.constraints=matrix(0, ncol=1, nrow=1)) )

Running Meta analysis with ML

Call:
meta(y = di, v = vi, data = Becker83, RE.constraints = matrix(0,
    ncol = 1, nrow = 1))

95% confidence intervals: z statistic approximation
Coefficients:
            Estimate Std.Error    lbound    ubound z value
Intercept1  0.100640  0.060510 -0.017957  0.219237  1.6632
           Pr(>|z|)
Intercept1  0.09627 .
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Q statistic on homogeneity of effect sizes: 30.64949
Degrees of freedom of the Q statistic: 9
P value of the Q statistic: 0.0003399239
Heterogeneity indices (based on the estimated Tau2):
                             Estimate
Intercept1: I2 (Q statistic)        0

Number of studies (or clusters): 10
```

```
Number of observed statistics: 10
Number of estimated parameters: 1
Degrees of freedom: 9
-2 log likelihood: 17.86043
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

```
R> ## Exact the coefficients
R> coef(fixed1)
```

```
Intercept1
 0.1006404
```

```
R> ## Exact the sampling variance covariance matrix
R> vcov(fixed1)
```

```
            Intercept1
Intercept1 0.003661436
```

Multivariate random-effects model Multivariate meta-analysis can be fitted by specifying the multivariate effect sizes and its sampling covariance matrix in the arguments `y` and `v` with `cbind()`, respectively. Only the lower triangle of the sampling covariance matrix arranged by the column major is used in `v`.

The Q statistic ($df = 8$) of the following example is 128.2267, $p < .001$. The pooled effect sizes with their 95% Wald CIs based on the random-effects model for PD and AL are 0.3448 (0.2397, 0.4500) and -0.3379 (-0.4972, -0.1787), respectively. The estimated variance component is $\left[\begin{array}{ll} 0.0070 & \\ 0.0095 & 0.02614 \end{array}\right]$. The I^2 based on the Q statistic for PD and AL are .6021 and .9250, respectively.

```
R> ## Show the data set
R> Berkey98
```

```
  trial pub_year no_of_patients   PD    AL var_PD cov_PD_AL
1     1     1983             14 0.47 -0.32 0.0075    0.0030
2     2     1982             15 0.20 -0.60 0.0057    0.0009
3     3     1979             78 0.40 -0.12 0.0021    0.0007
4     4     1987             89 0.26 -0.31 0.0029    0.0009
5     5     1988             16 0.56 -0.39 0.0148    0.0072
  var_AL
1 0.0077
2 0.0008
3 0.0014
4 0.0015
5 0.0304
```

```
R> ## Multivariate meta-analysis with a random-effects model
R> summary( mult1 <- meta(y=cbind(PD, AL), v=cbind(var_PD, cov_PD_AL, var_AL),
                          data=Berkey98) )

Running Meta analysis with ML

Call:
meta(y = cbind(PD, AL), v = cbind(var_PD, cov_PD_AL, var_AL),
    data = Berkey98)

95% confidence intervals: z statistic approximation
Coefficients:
             Estimate  Std.Error     lbound     ubound
Intercept1  0.3448392  0.0536312  0.2397239  0.4499544
Intercept2 -0.3379381  0.0812480 -0.4971812 -0.1786951
Tau2_1_1    0.0070020  0.0090497 -0.0107351  0.0247391
Tau2_2_1    0.0094607  0.0099698 -0.0100797  0.0290010
Tau2_2_2    0.0261445  0.0177409 -0.0086270  0.0609161
           z value  Pr(>|z|)
Intercept1  6.4298 1.278e-10 ***
Intercept2 -4.1593 3.192e-05 ***
Tau2_1_1    0.7737    0.4391
Tau2_2_1    0.9489    0.3427
Tau2_2_2    1.4737    0.1406
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Q statistic on homogeneity of effect sizes: 128.2267
Degrees of freedom of the Q statistic: 8
P value of the Q statistic: 0
Heterogeneity indices (based on the estimated Tau2):
                             Estimate
Intercept1: I2 (Q statistic)   0.6021
Intercept2: I2 (Q statistic)   0.9250

Number of studies (or clusters): 5
Number of observed statistics: 10
Number of estimated parameters: 5
Degrees of freedom: 5
-2 log likelihood: -11.68131
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Exact the coefficients
R> coef(mult1)

  Intercept1   Intercept2     Tau2_1_1     Tau2_2_1
 0.344839167 -0.337938117  0.007001998  0.009460665
```

```
   Tau2_2_2
 0.026144517

R> ## Exact the sampling variance covariance matrix
R> vcov(mult1)

              Intercept1   Intercept2     Tau2_1_1
Intercept1  2.876307e-03 2.215623e-03 1.241471e-04
Intercept2  2.215623e-03 6.601230e-03 6.203168e-05
Tau2_1_1    1.241471e-04 6.203168e-05 8.189758e-05
Tau2_2_1   -1.684464e-05 1.220432e-04 5.825516e-05
Tau2_2_2    1.315804e-06 3.246241e-05 4.503124e-05
                Tau2_2_1     Tau2_2_2
Intercept1 -1.684464e-05 1.315804e-06
Intercept2  1.220432e-04 3.246241e-05
Tau2_1_1    5.825516e-05 4.503124e-05
Tau2_2_1    9.939612e-05 1.187750e-04
Tau2_2_2    1.187750e-04 3.147402e-04
```

Multivariate mixed-effects model As an illustration, we use *pub_year* as a predictor. To make the intercept more interpretable, we center the publication year at 1979, the first record of publication year in the data set. The estimated regression coefficients and their 95% CIs on PD and AL are 0.0064 (-0.2048, 0.2177) and -0.0706 (-0.3883, 0.2471), respectively. The R^2 in predicting PD and AL are .0000 and .0433, respectively. The likelihood ratio statistic on testing both regression coefficient is $\chi^2(df = 2) = 0.3273, p = .8490$. Thus, both regression coefficients are non-significant.

Sometimes, we may want to test the equality of the regression coefficients and see if they are differnt. We may impose the equality constraint on the regression coefficients with the argument `coef.constraints`. The average regression coefficient is 0.0017 (-0.1991, 0.2025). The likelihood ratio statistic on testing the equality of the regression coefficients is $\chi^2(df = 1) = 0.3270, p = .5674$. There is no evidence that one regression coefficient is stronger from the other.

```
R> ## Multivariate meta-analysis with "publication year-1979" as a predictor
R> mult2 <- meta(y=cbind(PD, AL), v=cbind(var_PD, cov_PD_AL, var_AL), data=Berkey98,
               x=scale(pub_year, center=1979), model.name="No constraint")

Running No constraint

R> summary(mult2)

Call:
meta(y = cbind(PD, AL), v = cbind(var_PD, cov_PD_AL, var_AL),
    x = scale(pub_year, center = 1979), data = Berkey98, model.name = "No constraint")

95% confidence intervals: z statistic approximation
```

```
Coefficients:
             Estimate  Std.Error     lbound     ubound
Intercept1  0.3440001  0.0857659  0.1759020  0.5120982
Slope1_1    0.0063540  0.1078235 -0.2049761  0.2176842
Intercept2 -0.2918175  0.1312797 -0.5491208 -0.0345141
Slope2_1   -0.0705887  0.1620966 -0.3882922  0.2471147
Tau2_1_1    0.0080405  0.0101206 -0.0117955  0.0278766
Tau2_2_1    0.0093413  0.0105515 -0.0113392  0.0300218
Tau2_2_2    0.0250135  0.0170788 -0.0084603  0.0584873
           z value  Pr(>|z|)
Intercept1  4.0109 6.048e-05 ***
Slope1_1    0.0589   0.95301
Intercept2 -2.2229   0.02622 *
Slope2_1   -0.4355   0.66322
Tau2_1_1    0.7945   0.42692
Tau2_2_1    0.8853   0.37599
Tau2_2_2    1.4646   0.14303
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Q statistic on homogeneity of effect sizes: 128.2267
Degrees of freedom of the Q statistic: 8
P value of the Q statistic: 0
Explained variances (R2):
                           Estimate
y1: Tau2 (no predictor)      0.0070
y1: Tau2 (with predictors)   0.0080
y1: R2                       0.0000
y2: Tau2 (no predictor)      0.0261
y2: Tau2 (with predictors)   0.0250
y2: R2                       0.0433

Number of studies (or clusters): 5
Number of observed statistics: 10
Number of estimated parameters: 7
Degrees of freedom: 3
-2 log likelihood: -12.00859
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

```
R> ## Exact the coefficients
R> coef(mult2)
```

```
  Intercept1   Intercept2     Slope1_1     Slope2_1 
 0.344000113 -0.291817459  0.006354034 -0.070588746 
    Tau2_1_1     Tau2_2_1     Tau2_2_2 
 0.008040540  0.009341319  0.025013487 
```

```
R> ## Exact the sampling variance covariance matrix
R> vcov(mult2)

              Intercept1    Intercept2      Slope1_1
Intercept1  7.355789e-03  6.628461e-03 -7.148841e-03
Intercept2  6.628461e-03  1.723435e-02 -6.290031e-03
Slope1_1   -7.148841e-03 -6.290031e-03  1.162591e-02
Slope2_1   -6.692079e-03 -1.692509e-02  9.550531e-03
Tau2_1_1   -1.288708e-04 -2.379371e-05  3.800441e-04
Tau2_2_1   -1.307349e-04 -5.734270e-05  1.944444e-04
Tau2_2_2   -2.517793e-05 -4.989090e-06  4.768716e-05
                Slope2_1      Tau2_1_1      Tau2_2_1
Intercept1 -0.0066920794 -1.288708e-04 -1.307349e-04
Intercept2 -0.0169250890 -2.379371e-05 -5.734270e-05
Slope1_1    0.0095505309  3.800441e-04  1.944444e-04
Slope2_1    0.0262752958  1.400374e-04  2.907864e-04
Tau2_1_1    0.0001400374  1.024271e-04  7.161024e-05
Tau2_2_1    0.0002907864  7.161024e-05  1.113334e-04
Tau2_2_2    0.0001142197  4.726642e-05  1.186402e-04
                Tau2_2_2
Intercept1 -2.517793e-05
Intercept2 -4.989090e-06
Slope1_1    4.768716e-05
Slope2_1    1.142197e-04
Tau2_1_1    4.726642e-05
Tau2_2_1    1.186402e-04
Tau2_2_2    2.916845e-04

R> ## Multivariate meta-analysis with both regression coefficients fixed at 0
R> mult0 <- meta(y=cbind(PD, AL), v=cbind(var_PD, cov_PD_AL, var_AL), data=Berkey98,
                x=scale(pub_year, center=1979),
                model.name="Both regression coefficients fixed at 0",
                coef.constraints=matrix(c("0", "0"), nrow=2))

Running Both regression coefficients fixed at 0

R> summary(mult0)

Call:
meta(y = cbind(PD, AL), v = cbind(var_PD, cov_PD_AL, var_AL),
    x = scale(pub_year, center = 1979), data = Berkey98, coef.constraints = matrix(c("0",
        "0"), nrow = 2), model.name = "Both regression coefficients fixed at 0")

95% confidence intervals: z statistic approximation
Coefficients:
             Estimate  Std.Error     lbound     ubound
```

```
Intercept1  0.3448392  0.0536312  0.2397239  0.4499544
Intercept2 -0.3379381  0.0812480 -0.4971812 -0.1786951
Tau2_1_1    0.0070020  0.0090497 -0.0107351  0.0247391
Tau2_2_1    0.0094607  0.0099698 -0.0100797  0.0290010
Tau2_2_2    0.0261445  0.0177409 -0.0086270  0.0609161
           z value  Pr(>|z|)
Intercept1  6.4298 1.278e-10 ***
Intercept2 -4.1593 3.192e-05 ***
Tau2_1_1    0.7737    0.4391
Tau2_2_1    0.9489    0.3427
Tau2_2_2    1.4737    0.1406
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Q statistic on homogeneity of effect sizes: 128.2267
Degrees of freedom of the Q statistic: 8
P value of the Q statistic: 0
Explained variances (R2):
                           Estimate
y1: Tau2 (no predictor)      0.0070
y1: Tau2 (with predictors)   0.0070
y1: R2                       0.0000
y2: Tau2 (no predictor)      0.0261
y2: Tau2 (with predictors)   0.0261
y2: R2                       0.0000

Number of studies (or clusters): 5
Number of observed statistics: 10
Number of estimated parameters: 5
Degrees of freedom: 5
-2 log likelihood: -11.68131
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Likelihood ratio test on testing both regression coefficients are 0
R> anova(mult2, mult0)

           base                              comparison ep
1 No constraint                                    <NA>  7
2 No constraint Both regression coefficients fixed at 0  5
   minus2LL df       AIC    diffLL diffdf         p
1 -12.00859  3 -18.00859        NA     NA        NA
2 -11.68131  5 -21.68131 0.3272789      2 0.8490481

R> ## Multivariate meta-analysis with an equality constraint on the slopes
R> mult3 <- meta(y=cbind(PD, AL), v=cbind(var_PD, cov_PD_AL, var_AL), data=Berkey98,
               x=scale(pub_year, center=1979), model.name="With equality constraint",
               coef.constraints=matrix(c("0.3*Equal_Slope", "0.3*Equal_Slope"), nrow=2))
```

```
Running With equality constraint

R> summary(mult3)

Call:
meta(y = cbind(PD, AL), v = cbind(var_PD, cov_PD_AL, var_AL),
    x = scale(pub_year, center = 1979), data = Berkey98, coef.constraints = matrix(c("0.3*
        "0.3*Equal_Slope"), nrow = 2), model.name = "With equality constraint")

95% confidence intervals: z statistic approximation
Coefficients:
              Estimate  Std.Error     lbound     ubound
Intercept1   0.3437612  0.0849828  0.1771980  0.5103245
Equal_Slope  0.0016745  0.1024442 -0.1991124  0.2024614
Intercept2  -0.3390010  0.1041005 -0.5430343 -0.1349678
Tau2_1_1     0.0070474  0.0094638 -0.0115013  0.0255961
Tau2_2_1     0.0095164  0.0105668 -0.0111940  0.0302269
Tau2_2_2     0.0261979  0.0180773 -0.0092330  0.0616287
            z value  Pr(>|z|)
Intercept1   4.0451 5.231e-05 ***
Equal_Slope  0.0163  0.986958
Intercept2  -3.2565  0.001128 **
Tau2_1_1     0.7447  0.456472
Tau2_2_1     0.9006  0.367800
Tau2_2_2     1.4492  0.147278
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Q statistic on homogeneity of effect sizes: 128.2267
Degrees of freedom of the Q statistic: 8
P value of the Q statistic: 0
Explained variances (R2):
                           Estimate
y1: Tau2 (no predictor)      0.0070
y1: Tau2 (with predictors)   0.0070
y1: R2                       0.0000
y2: Tau2 (no predictor)      0.0261
y2: Tau2 (with predictors)   0.0262
y2: R2                       0.0000

Number of studies (or clusters): 5
Number of observed statistics: 10
Number of estimated parameters: 6
Degrees of freedom: 4
-2 log likelihood: -11.68158
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

```
R> ## Exact the coefficients
R> coef(mult3)

  Intercept1   Intercept2  Equal_Slope     Tau2_1_1
 0.343761239 -0.339001019  0.001674542  0.007047407
    Tau2_2_1     Tau2_2_2
 0.009516440  0.026197856

R> ## Exact the sampling variance covariance matrix
R> vcov(mult3)

               Intercept1    Intercept2   Equal_Slope
Intercept1   7.222075e-03  0.0065104549 -0.0067506847
Intercept2   6.510455e-03  0.0108369149 -0.0066601781
Equal_Slope -6.750685e-03 -0.0066601781  0.0104948091
Tau2_1_1    -6.400934e-05 -0.0001221578  0.0002892786
Tau2_2_1    -2.447019e-04 -0.0001027742  0.0003530272
Tau2_2_2    -2.159290e-04 -0.0001825541  0.0003374792
                 Tau2_1_1      Tau2_2_1      Tau2_2_2
Intercept1  -6.400934e-05 -2.447019e-04 -2.159290e-04
Intercept2  -1.221578e-04 -1.027742e-04 -1.825541e-04
Equal_Slope  2.892786e-04  3.530272e-04  3.374792e-04
Tau2_1_1     8.956372e-05  6.810625e-05  5.473181e-05
Tau2_2_1     6.810625e-05  1.116565e-04  1.308804e-04
Tau2_2_2     5.473181e-05  1.308804e-04  3.267891e-04

R> ## Likelihood ratio test on the equality of regression coefficients
R> anova(mult2, mult3)

           base                comparison ep  minus2LL df
1 No constraint                      <NA>  7 -12.00859  3
2 No constraint With equality constraint  6 -11.68158  4
        AIC    diffLL diffdf         p
1 -18.00859        NA     NA        NA
2 -19.68158 0.3270107      1 0.5674246
```

Multivariate fixed-effects model A multivariate fixed-effects meta-analysis can be conducted by fixing the variance component at a zero matrix. The following code illustrates the syntax.

```
R> ## Multivariate meta-analysis with a fixed-effects model
R> summary( mult4 <- meta(y=cbind(PD, AL), v=cbind(var_PD, cov_PD_AL, var_AL),
                         data=Berkey98,
                         RE.constraints=matrix(0, nrow=2, ncol=2)) )
```

```
Running Meta analysis with ML

Call:
meta(y = cbind(PD, AL), v = cbind(var_PD, cov_PD_AL, var_AL),
    data = Berkey98, RE.constraints = matrix(0, nrow = 2, ncol = 2))

95% confidence intervals: z statistic approximation
Coefficients:
            Estimate Std.Error    lbound    ubound z value
Intercept1  0.307219  0.028575  0.251212  0.363225  10.751
Intercept2 -0.394377  0.018649 -0.430929 -0.357825 -21.147
            Pr(>|z|)
Intercept1 < 2.2e-16 ***
Intercept2 < 2.2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Q statistic on homogeneity of effect sizes: 128.2267
Degrees of freedom of the Q statistic: 8
P value of the Q statistic: 0
Heterogeneity indices (based on the estimated Tau2):
                             Estimate
Intercept1: I2 (Q statistic)        0
Intercept2: I2 (Q statistic)        0

Number of studies (or clusters): 5
Number of observed statistics: 10
Number of estimated parameters: 2
Degrees of freedom: 8
-2 log likelihood: 90.88326
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Exact the coefficients
R> coef(mult4)

Intercept1 Intercept2
 0.3072186 -0.3943770

R> ## Exact the sampling variance covariance matrix
R> vcov(mult4)

             Intercept1   Intercept2
Intercept1 0.0008165393 0.0002072041
Intercept2 0.0002072041 0.0003477936
```

REML The `reml()` function may be used to estimate the variance component with the REML estimation method. It should be noted that it does not estimate the fixed-effects. The fixed-effects estimates can be obtained via the `meta()` function by specifying the estimated variance component from `reml()` as fixed values in the `RE.constraints` argument. This approach is consistent with the idea of REML that removes the fixed-effects parameter when estimating the variance component.

```
R> ## Random-effects meta-analysis with ML
R> summary( meta(y=di, v=vi, data=Becker83) )

Running Meta analysis with ML

Call:
meta(y = di, v = vi, data = Becker83)

95% confidence intervals: z statistic approximation
Coefficients:
            Estimate Std.Error    lbound    ubound z value
Intercept1  0.174734  0.113378 -0.047482  0.396950  1.5412
Tau2_1_1    0.077376  0.054108 -0.028674  0.183426  1.4300
           Pr(>|z|)
Intercept1   0.1233
Tau2_1_1     0.1527

Q statistic on homogeneity of effect sizes: 30.64949
Degrees of freedom of the Q statistic: 9
P value of the Q statistic: 0.0003399239
Heterogeneity indices (based on the estimated Tau2):
                             Estimate
Intercept1: I2 (Q statistic)   0.6718

Number of studies (or clusters): 10
Number of observed statistics: 10
Number of estimated parameters: 2
Degrees of freedom: 8
-2 log likelihood: 7.928307
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Random-effects meta-analysis with REML
R> summary( VarComp <- reml(y=di, v=vi, data=Becker83) )

Running Variance component with REML

Call:
reml(y = di, v = vi, data = Becker83)

95% confidence intervals: z statistic approximation
Coefficients:
          Estimate Std.Error    lbound    ubound z value
```

```
Tau2_1_1  0.091445  0.064228 -0.034439  0.217329  1.4238
         Pr(>|z|)
Tau2_1_1   0.1545

Number of studies (or clusters): 10
Number of observed statistics: 9
Number of estimated parameters: 1
Degrees of freedom: 8
-2 log likelihood: -6.110579
OpenMx status: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Extract the variance component
R> VarComp_REML <- matrix( coef(VarComp), ncol=1, nrow=1 )
R> ## Meta-analysis by treating the variance component as fixed
R> summary( meta(y=di, v=vi, data=Becker83, RE.constraints=VarComp_REML) )

Running Meta analysis with ML

Call:
meta(y = di, v = vi, data = Becker83, RE.constraints = VarComp_REML)

95% confidence intervals: z statistic approximation
Coefficients:
            Estimate Std.Error    lbound    ubound z value
Intercept1  0.180189  0.117535 -0.050176  0.410555  1.5331
           Pr(>|z|)
Intercept1   0.1253

Q statistic on homogeneity of effect sizes: 30.64949
Degrees of freedom of the Q statistic: 9
P value of the Q statistic: 0.0003399239
Heterogeneity indices (based on the estimated Tau2):
                             Estimate
Intercept1: I2 (Q statistic)   0.7075

Number of studies (or clusters): 10
Number of observed statistics: 10
Number of estimated parameters: 1
Degrees of freedom: 9
-2 log likelihood: 7.986161
OpenMx status1: 1 ("0" and "1": considered fine; other values indicate problems)

R> ## Estimate variance components with REML
R> summary( reml(y=di, v=vi, x=log(items), data=Becker83) )

Running Variance component with REML
```

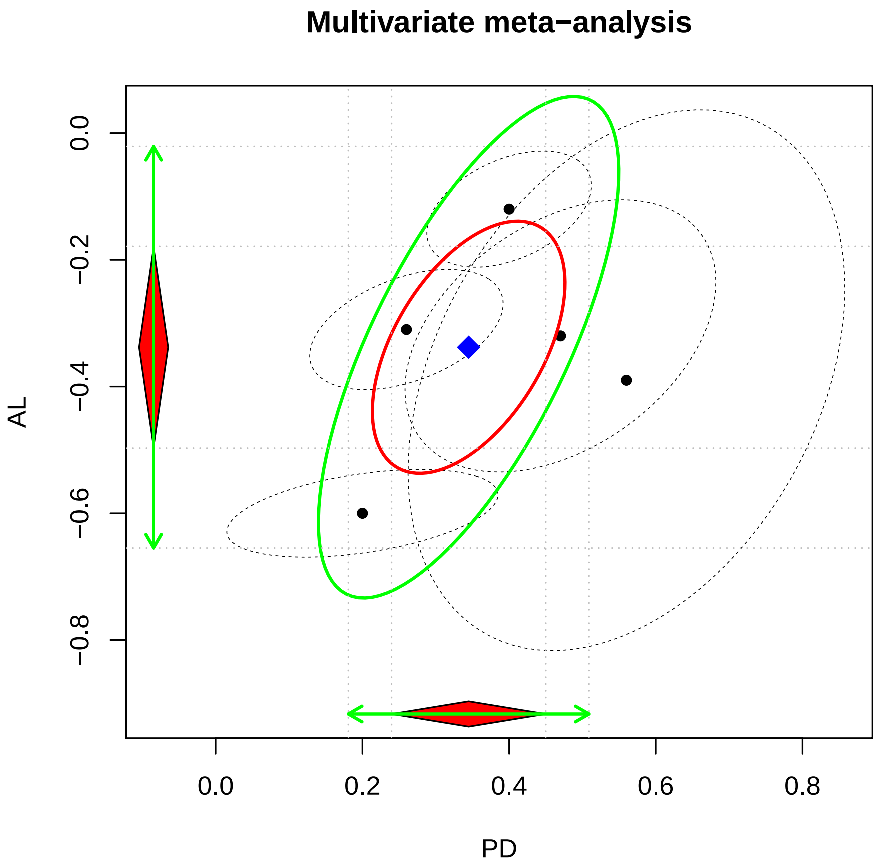
```
Call:
reml(y = di, v = vi, x = log(items), data = Becker83)

95% confidence intervals: z statistic approximation
Coefficients:
           Estimate  Std.Error     lbound     ubound
Tau2_1_1  0.0052656  0.0212014 -0.0362884  0.0468196
         z value Pr(>|z|)
Tau2_1_1  0.2484   0.8039

Number of studies (or clusters): 10
Number of observed statistics: 8
Number of estimated parameters: 1
Degrees of freedom: 7
-2 log likelihood: -10.84567
OpenMx status: 0 ("0" and "1": considered fine; other values indicate problems)
```

```
R> ## Estimate variance components with REML
R> summary( reml(y=cbind(PD, AL), v=cbind(var_PD, cov_PD_AL, var_AL), data=Berkey98) )

Running Variance component with REML

Call:
reml(y = cbind(PD, AL), v = cbind(var_PD, cov_PD_AL, var_AL),
    data = Berkey98)

95% confidence intervals: z statistic approximation
Coefficients:
          Estimate Std.Error    lbound    ubound z value
Tau2_1_1  0.011733  0.013645 -0.015011  0.038477  0.8599
Tau2_2_1  0.011916  0.014416 -0.016340  0.040172  0.8266
Tau2_2_2  0.032651  0.024402 -0.015176  0.080479  1.3380
         Pr(>|z|)
Tau2_1_1   0.3899
Tau2_2_1   0.4085
Tau2_2_2   0.1809

Number of studies (or clusters): 5
Number of observed statistics: 8
Number of estimated parameters: 3
Degrees of freedom: 5
-2 log likelihood: -18.86768
OpenMx status: 0 ("0" and "1": considered fine; other values indicate problems)
```

Plots of multivariate effect sizes If multivariate meta-analysis is conducted, pairwise plots on the pooled effect sizes and their confidence ellipses can be obtained via the `plot()`

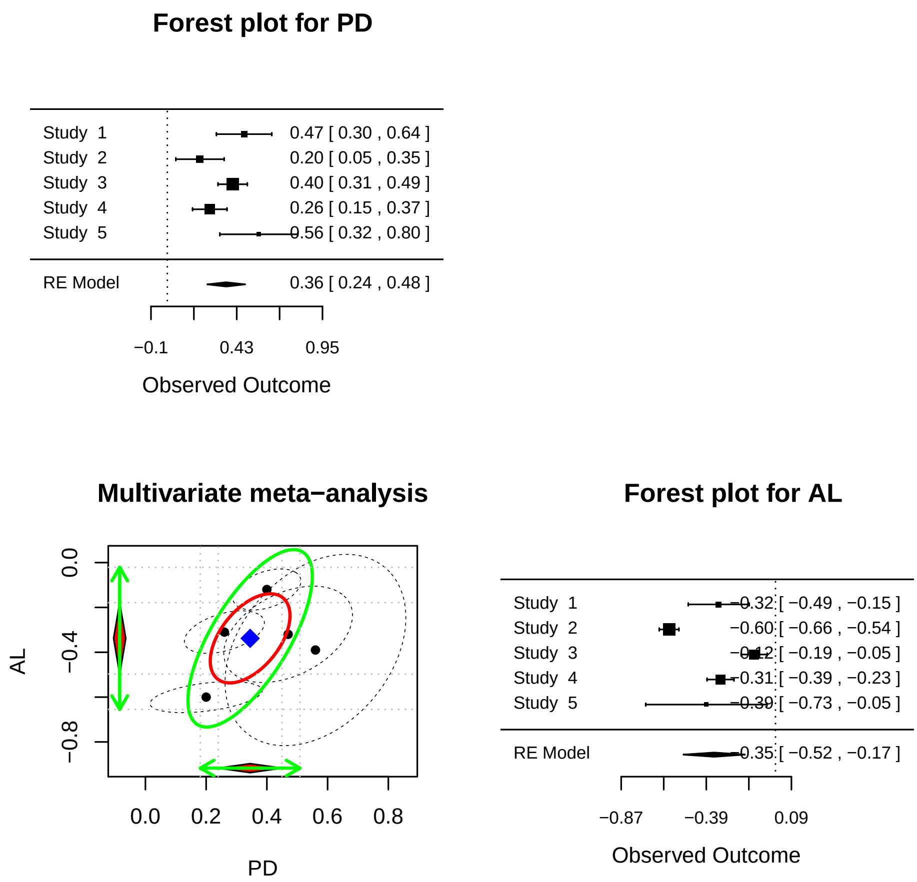
function. By default, 95% confidence intervals on the average effect sizes and confidence ellipses on the random effects are plotted. For example,

```
R> Berkey98.ma <- meta(y=cbind(PD, AL), v=cbind(var_PD, cov_PD_AL, var_AL), data=Berkey98)

Running Meta analysis with ML

R> plot(Berkey98.ma, main="Multivariate meta-analysis", axis.label=c("PD", "AL"))
```



By combining with the forest plots from the **metafor** package, we may combine the univariate and multivariate natures of the effect sizes in a single figure. This will be very useful for multivariate meta-analysis.

```
R> ## Load the metafor package to display forest plots
R> library(metafor)
R> plot(Berkey98.ma, diag.panel=TRUE, main="Multivariate meta-analysis",
        axis.label=c("PD", "AL"))
R> forest( rma(yi=PD, vi=var_PD, data=Berkey98) )
R> title("Forest plot for PD")
R> forest( rma(yi=AL, vi=var_AL, data=Berkey98) )
R> title("Forest plot for AL")
```



Three-level meta-analysis The `meta3()` function may be used to fit three-level meta-analytic models. It is assumed that effect sizes within `cluster` are dependent. The Q statistic ($df = 55$) of the following example is 578.864, $p < .001$. The I^2 at level-2 and level-3 are .3440 and .6043, respectively. The estimated coefficient of $Year$ of publication is 0.0051, $p = .5518$. The R^2 at level-2 and level-3 are .0000 and .0221, respectively.

```
R> ## ML estimation method
R> ## No predictor
R> summary( meta3(y=y, v=v, cluster=District, data=Cooper03) )

Running Meta analysis with ML

Call:
meta3(y = y, v = v, cluster = District, data = Cooper03)

95% confidence intervals: z statistic approximation
Coefficients:
           Estimate  Std.Error     lbound     ubound
Intercept 0.1844553  0.0805411  0.0265977  0.3423130
```

```
Tau2_2     0.0328648  0.0111397  0.0110314  0.0546982
Tau2_3     0.0577384  0.0307423 -0.0025154  0.1179921
          z value Pr(>|z|)
Intercept  2.2902 0.022010 *
Tau2_2     2.9502 0.003175 **
Tau2_3     1.8781 0.060362 .
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Q statistic on homogeneity of effect sizes: 578.864
Degrees of freedom of the Q statistic: 55
P value of the Q statistic: 0
Heterogeneity indices (based on the estimated Tau2):
                   Estimate
I2_2 (Q statistic)   0.3440
I2_3 (Q statistic)   0.6043

Number of studies (or clusters): 11
Number of observed statistics: 56
Number of estimated parameters: 3
Degrees of freedom: 53
-2 log likelihood: 16.78987
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Year as a predictor
R> summary( meta3(y=y, v=v, cluster=District, x=scale(Year, scale=FALSE), data=Cooper03) )

Running Meta analysis with ML

Call:
meta3(y = y, v = v, cluster = District, x = scale(Year, scale = FALSE),
    data = Cooper03)

95% confidence intervals: z statistic approximation
Coefficients:
            Estimate  Std.Error     lbound     ubound
Slope_1    0.0050737  0.0085266 -0.0116382  0.0217856
Intercept  0.1780268  0.0805219  0.0202067  0.3358469
Tau2_2     0.0329390  0.0111620  0.0110618  0.0548162
Tau2_3     0.0564628  0.0300330 -0.0024007  0.1153264
          z value Pr(>|z|)
Slope_1    0.5950 0.551814
Intercept  2.2109 0.027042 *
Tau2_2     2.9510 0.003168 **
Tau2_3     1.8800 0.060104 .
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
Q statistic on homogeneity of effect sizes: 578.864
Degrees of freedom of the Q statistic: 55
P value of the Q statistic: 0
Explained variances (R2):
                         Estimate
Tau2_2 (no predictor)      0.0329
Tau2_2 (with predictors)   0.0329
R2_2 (level-2)             0.0000
Tau2_3 (no predictor)      0.0577
Tau2_3 (with predictors)   0.0565
R2_3 (level-3)             0.0221

Number of studies (or clusters): 11
Number of observed statistics: 56
Number of estimated parameters: 4
Degrees of freedom: 52
-2 log likelihood: 16.43629
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

```
R> ## REML estimation method
R> ## No predictor; with LBCI
R> summary( reml3(y=y, v=v, cluster=District, data=Cooper03, intervals.type="LB") )
```

```
Running Variance component with REML

Call:
reml3(y = y, v = v, cluster = District, data = Cooper03, intervals.type = "LB")

95% confidence intervals: Likelihood-based statistic
Coefficients:
       Estimate Std.Error   lbound   ubound z value
Tau2_2 0.032737  0.011092 0.016264 0.062842  2.9513
Tau2_3 0.065062  0.035510 0.022234 0.207846  1.8322
       Pr(>|z|)
Tau2_2 0.003164 **
Tau2_3 0.066921 .
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Number of studies (or clusters): 56
Number of observed statistics: 55
Number of estimated parameters: 2
Degrees of freedom: 53
-2 log likelihood: -81.14044
OpenMx status: 0 ("0" and "1": considered fine; other values indicate problems)
```

```
R> ## Year as a predictor
R> summary( reml3(y=y, v=v, cluster=District, x=scale(Year, scale=FALSE), data=Cooper03) )

Running Variance component with REML

Call:
reml3(y = y, v = v, cluster = District, x = scale(Year, scale = FALSE),
    data = Cooper03)

95% confidence intervals: z statistic approximation
Coefficients:
        Estimate  Std.Error     lbound     ubound z value
Tau2_2  0.0326502  0.0110529  0.0109870  0.0543134  2.9540
Tau2_3  0.0722656  0.0405349 -0.0071813  0.1517125  1.7828
       Pr(>|z|)
Tau2_2 0.003137 **
Tau2_3 0.074619 .
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Number of studies (or clusters): 56
Number of observed statistics: 54
Number of estimated parameters: 2
Degrees of freedom: 52
-2 log likelihood: -72.09405
OpenMx status: 0 ("0" and "1": considered fine; other values indicate problems)
```

3. Meta-analytic structural equation modeling

MASEM combines the idea of meta-analysis and SEM by pooling correlation/covariance matrices and testing structural equation models on the pooled correlation/covariance matrix. There are two stages in conducting a MASEM. In the first stage the correlation/covariance matrices are pooled together. In the second stage, the pooled correlation/covariance matrix is used to fit structural equation models.

Cheung and Chan (2005b, 2009) proposed a two-stage structural equation modeling (TSSEM) based on a fixed-effects model. The `metaSEM` package has implemented the TSSEM approach. Moreover, the TSSEM approach has been extended to the random-effects model by using a multivariate meta-analysis (Cheung 2011b) in the first stage analysis. Regardless of whether a fixed- or random-effects model is used, the `tssem2()` function will handle this automatically. In other words, parameter estimates, standard errors and goodness-of-fit indices in the stage 2 analysis has already taken the stage 1 model into account.

An example from Cheung (2009b) is used to illustrate the procedures. In this example, Digman (1997) reported a second-order factor analysis on a five-factor model with 14 studies. He proposed that there were two second-order factors for the five-factor model: an alpha factor for agreeableness, conscientiousness, and emotional stability, and a beta factor for extroversion and intellect.

3.1. Fixed-effects model

The `tssem1()` function is used to pool the correlation matrices with a fixed-effects model in the first stage by specifying `method='FEM'` in the argument. `tssem2()` is then used to fit a factor analytic model on the pooled correlation matrix with the inverse of its asymptotic covariance matrix as the weight matrix (Cheung and Chan 2005b, 2009).

The fit indices for testing the homogeneity of the correlation matrices in Stage 1 analysis are $\chi^2(130, N = 4496) = 1499.73, p < .001$, CFI=0.6825, TLI=0.6581, SRMR=0.1750 and RMSEA=0.1812. This indicates that it is not reasonable to assume that the correlation matrices are homogenous. Sub-group analysis or random-effects model that will be illustrated later are more appropriate. As an exercise, we continute to fit the stage 2 model. The fit indices for fitting the structural model in Stage 2 are $\chi^2(4, N = 4496) = 67.89, p < .001$, CFI=0.9845, TLI=0.9613, SRMR=0.0285 and RMSEA=0.0596.

```
R> ## Show the first 2 studies in Digman97
R> head(Digman97$data, n=2)

$`Digman 1 (1994)`
       A     C   ES     E    I
A   1.00  0.62 0.41 -0.48 0.00
C   0.62  1.00 0.59 -0.10 0.35
ES  0.41  0.59 1.00  0.27 0.41
E  -0.48 -0.10 0.27  1.00 0.37
I   0.00  0.35 0.41  0.37 1.00

$`Digman 2 (1994)`
       A    C   ES     E     I
A   1.00 0.39 0.53 -0.30 -0.05
C   0.39 1.00 0.59  0.07  0.44
ES  0.53 0.59 1.00  0.09  0.22
E  -0.30 0.07 0.09  1.00  0.45
I  -0.05 0.44 0.22  0.45  1.00

R> ## Show the first 2 sample sizes in Digman97
R> head(Digman97$n, n=2)

[1] 102 149

R> ## Example of Fixed-effects TSSEM
R> fixed1 <- tssem1(Digman97$data, Digman97$n, method="FEM")

Running TSSEM1 Analysis of Correlation Matrix

R> summary(fixed1)

Call:
tssem1FEM(my.df = my.df, n = n, cor.analysis = cor.analysis,
```

```
    model.name = model.name, cluster = cluster, suppressWarnings = suppressWarnings)

Coefficients:
       Estimate Std.Error z value  Pr(>|z|)
S[1,2] 0.363116  0.013390 27.1174 < 2.2e-16 ***
S[1,3] 0.390176  0.012903 30.2394 < 2.2e-16 ***
S[1,4] 0.103751  0.015070  6.8846 5.794e-12 ***
S[1,5] 0.092246  0.015071  6.1207 9.316e-10 ***
S[2,3] 0.415999  0.012540 33.1744 < 2.2e-16 ***
S[2,4] 0.135208  0.014799  9.1363 < 2.2e-16 ***
S[2,5] 0.141213  0.014891  9.4834 < 2.2e-16 ***
S[3,4] 0.244505  0.014175 17.2488 < 2.2e-16 ***
S[3,5] 0.138167  0.014858  9.2992 < 2.2e-16 ***
S[4,5] 0.424514  0.012396 34.2466 < 2.2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Goodness-of-fit indices:
                                     Value
Sample size                      4496.0000
Chi-square of target model       1499.7340
DF of target model                130.0000
p value of target model             0.0000
Chi-square of independent model 4454.5995
DF of independent model           140.0000
RMSEA                               0.1812
SRMR                                0.1750
TLI                                 0.6581
CFI                                 0.6825
AIC                              1239.7340
BIC                               406.3114
OpenMx status: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Extract the pooled correlation matrix
R> coef(fixed1)

           x1        x2        x3        x4         x5
x1 1.00000000 0.3631157 0.3901765 0.1037511 0.09224586
x2 0.36311572 1.0000000 0.4159987 0.1352076 0.14121294
x3 0.39017646 0.4159987 1.0000000 0.2445051 0.13816667
x4 0.10375113 0.1352076 0.2445051 1.0000000 0.42451421
x5 0.09224586 0.1412129 0.1381667 0.4245142 1.00000000

R> ## Exact the sampling variance covariance matrix
R> vcov(fixed1)

             x2 x1        x3 x1        x4 x1        x5 x1
x2 x1 1.469907e-04 3.838613e-05 1.459870e-05 1.738852e-05
```

```
x3 x1 3.838613e-05 1.380993e-04 3.291322e-05 1.593040e-05
x4 x1 1.459870e-05 3.291322e-05 2.131330e-04 8.828891e-05
x5 x1 1.738852e-05 1.593040e-05 8.828891e-05 2.160834e-04
x3 x2 3.188759e-05 2.548896e-05 6.819538e-06 5.068077e-06
x4 x2 7.181122e-06 5.714476e-06 7.178708e-05 2.902241e-05
x5 x2 5.973882e-06 2.980482e-06 2.891491e-05 7.375722e-05
x4 x3 1.147757e-06 9.431105e-07 7.186433e-05 2.930447e-05
x5 x3 3.714609e-06 5.377907e-06 2.994837e-05 7.926245e-05
x5 x4 4.522226e-07 8.036684e-07 7.138436e-06 9.757525e-06
             x3 x2        x4 x2        x5 x2        x4 x3
x2 x1 3.188759e-05 7.181122e-06 5.973882e-06 1.147757e-06
x3 x1 2.548896e-05 5.714476e-06 2.980482e-06 9.431105e-07
x4 x1 6.819538e-06 7.178708e-05 2.891491e-05 7.186433e-05
x5 x1 5.068077e-06 2.902241e-05 7.375722e-05 2.930447e-05
x3 x2 1.292690e-04 2.905738e-05 1.189870e-05 4.659802e-06
x4 x2 2.905738e-05 2.083179e-04 8.423570e-05 7.495569e-05
x5 x2 1.189870e-05 8.423570e-05 2.092633e-04 3.026949e-05
x4 x3 4.659802e-06 7.495569e-05 3.026949e-05 1.859687e-04
x5 x3 1.248480e-05 3.164628e-05 8.223973e-05 7.646729e-05
x5 x4 1.707692e-06 1.252276e-05 1.126839e-05 4.745070e-06
             x5 x3        x5 x4
x2 x1 3.714609e-06 4.522226e-07
x3 x1 5.377907e-06 8.036684e-07
x4 x1 2.994837e-05 7.138436e-06
x5 x1 7.926245e-05 9.757525e-06
x3 x2 1.248480e-05 1.707692e-06
x4 x2 3.164628e-05 1.252276e-05
x5 x2 8.223973e-05 1.126839e-05
x4 x3 7.646729e-05 4.745070e-06
x5 x3 2.077769e-04 2.841400e-05
x5 x4 2.841400e-05 1.270258e-04
```

```
R> ## S matrix
R> Phi <- matrix(c(1,"0.3*cor","0.3*cor",1), ncol=2, nrow=2)
R> S1 <- bdiagMat(list(diag(c("0.2*e1","0.2*e2","0.2*e3","0.2*e4","0.2*e5")), Phi))
R> S1 <- as.mxMatrix(S1)
R> ## A matrix
R> Lambda <- matrix(c(0,".3*f1_x2",".3*f1_x3",".3*f1_x4",0,".3*f2_x1",0,0,0,".3*f2_x5"),
                   ncol=2, nrow=5)
R> A1 <- rbind( cbind(matrix(0,ncol=5,nrow=5), Lambda),
               matrix(0, ncol=7, nrow=2) )
R> A1 <- as.mxMatrix(A1)
R> F1 <- create.Fmatrix(c(1,1,1,1,1,0,0), name="F1")
R> fixed2 <- tssem2(fixed1, Amatrix=A1, Smatrix=S1, Fmatrix=F1, diag.constraints=TRUE, int
                   model.name="TSSEM2 Digman97")
```

```
Running TSSEM2 Digman97
```

```
R> summary(fixed2)

Call:
wls(Cov = tssem1.obj$pooledS, asyCov = tssem1.obj$acovS, n = tssem1.obj$total.n,
    Amatrix = Amatrix, Smatrix = Smatrix, Fmatrix = Fmatrix,
    diag.constraints = diag.constraints, cor.analysis = cor.analysis,
    intervals.type = intervals.type, model.name = model.name,
    suppressWarnings = suppressWarnings)

95% confidence intervals: Likelihood-based statistic
Coefficients:
             Estimate Std.Error  lbound  ubound z value
Amatrix[1,7]  0.48934        NA 0.45743 0.52098      NA
Amatrix[2,6]  0.57156        NA 0.54692 0.59628      NA
Amatrix[3,6]  0.66392        NA 0.64030 0.68769      NA
Amatrix[4,6]  0.58220        NA 0.55545 0.60895      NA
Amatrix[5,7]  0.48476        NA 0.45134 0.51790      NA
Smatrix[1,1]  0.76055        NA 0.72858 0.79076      NA
Smatrix[2,2]  0.67332        NA 0.64445 0.70088      NA
Smatrix[3,3]  0.55921        NA 0.52708 0.59001      NA
Smatrix[4,4]  0.66105        NA 0.62917 0.69147      NA
Smatrix[5,5]  0.76501        NA 0.73178 0.79629      NA
Smatrix[7,6]  1.08026        NA 1.02716 1.14018      NA
             Pr(>|z|)
Amatrix[1,7]       NA
Amatrix[2,6]       NA
Amatrix[3,6]       NA
Amatrix[4,6]       NA
Amatrix[5,7]       NA
Smatrix[1,1]       NA
Smatrix[2,2]       NA
Smatrix[3,3]       NA
Smatrix[4,4]       NA
Smatrix[5,5]       NA
Smatrix[7,6]       NA

Goodness-of-fit indices:
                                               Value
Sample size                                4496.0000
Chi-square of target model                  706.3461
DF of target model                            4.0000
p value of target model                       0.0000
Number of constraints imposed on "Smatrix"    5.0000
DF manually adjusted                          0.0000
Chi-square of independent model            4132.8584
DF of independent model                      10.0000
RMSEA                                         0.1976
```

```
SRMR                                            0.1455
TLI                                             0.5741
CFI                                             0.8296
AIC                                           698.3461
BIC                                           672.7023
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

Example: Fixed-effects model with sub-group analysis Studies may not share the same population correlation matrix. If the studies can be grouped into various subgroups, we may pool the correlation matrices separately by the subgroups (Cheung and Chan 2005a). This is similar to the subgroup analysis in conventional meta-analysis (Hedges and Olkin 1985). For example, Digman (1997) groups the 14 studies into several groups according to their sample characteristics. These include children, adolescents, young adults, and mature adults. This variable is stored in the variable `Digman97$cluster`. We may further group these studies into younger participants versus older participants. Separate fixed-effects analysis may be applied into these two groups.

The following R code may be used to conduct the analysis. Users have to supply the cluster (a vector of labels) to the `cluster` argument in `tssem1()`. The correlation/covariance matrices will be pooled separately for each cluster. The structural models will also be fitted separately for each cluster.

```
R> #### Create a variable for different samples
R> #### Younger participants: Children and Adolescents
R> #### Older participants: others
R> sample <- ifelse(Digman97$cluster %in% c("Children","Adolescents"),
                   yes="Younger participants", no="Older participants")
R> #### Show the sample
R> sample

 [1] "Younger participants" "Younger participants"
 [3] "Younger participants" "Younger participants"
 [5] "Younger participants" "Older participants"
 [7] "Older participants"   "Older participants"
 [9] "Older participants"   "Older participants"
[11] "Older participants"   "Older participants"
[13] "Older participants"   "Older participants"

R> ## Example of Fixed-effects TSSEM with several clusters
R> fixed1.cluster <- tssem1(Digman97$data, Digman97$n, method="FEM",
                           cluster=sample)

Running TSSEM1 Analysis of Correlation Matrix
Running TSSEM1 Analysis of Correlation Matrix

R> #### Please note that the estimates for the younger participants are problematic.
R> summary(fixed1.cluster)
```

```
$`Older participants`

Call:
tssem1FEM(my.df = data.cluster[[i]], n = n.cluster[[i]], cor.analysis = cor.analysis,
    model.name = model.name, suppressWarnings = suppressWarnings)

Coefficients:
       Estimate Std.Error z value  Pr(>|z|)
S[1,2] 0.297484  0.015455 19.2487 < 2.2e-16 ***
S[1,3] 0.370088  0.014552 25.4321 < 2.2e-16 ***
S[1,4] 0.137688  0.016423  8.3838 < 2.2e-16 ***
S[1,5] 0.097971  0.016744  5.8510 4.886e-09 ***
S[2,3] 0.393709  0.014163 27.7981 < 2.2e-16 ***
S[2,4] 0.182984  0.016075 11.3831 < 2.2e-16 ***
S[2,5] 0.092664  0.016664  5.5609 2.684e-08 ***
S[3,4] 0.260756  0.015573 16.7443 < 2.2e-16 ***
S[3,5] 0.096063  0.016594  5.7890 7.079e-09 ***
S[4,5] 0.411753  0.013917 29.5857 < 2.2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Goodness-of-fit indices:
                                    Value
Sample size                     3658.0000
Chi-square of target model       823.8769
DF of target model                80.0000
p value of target model            0.0000
Chi-square of independent model 2992.9294
DF of independent model           90.0000
RMSEA                              0.1513
SRMR                               0.1528
TLI                                0.7117
CFI                                0.7437
AIC                              663.8769
BIC                              167.5032
OpenMx status: 0 ("0" and "1": considered fine; other values indicate problems)

$`Younger participants`

Call:
tssem1FEM(my.df = data.cluster[[i]], n = n.cluster[[i]], cor.analysis = cor.analysis,
    model.name = model.name, suppressWarnings = suppressWarnings)

Coefficients:
        Estimate Std.Error z value  Pr(>|z|)
S[1,2]  0.604396  0.022189 27.2391 < 2.2e-16 ***
S[1,3]  0.465441  0.027579 16.8768 < 2.2e-16 ***
```

```
S[1,4] -0.030869  0.036047 -0.8563   0.39181
S[1,5]  0.061581  0.034650  1.7772   0.07553 .
S[2,3]  0.501309  0.026431 18.9668 < 2.2e-16 ***
S[2,4] -0.060834  0.034660 -1.7552   0.07923 .
S[2,5]  0.321019  0.031156 10.3035 < 2.2e-16 ***
S[3,4]  0.175422  0.033776  5.1937 2.061e-07 ***
S[3,5]  0.305214  0.031679  9.6345 < 2.2e-16 ***
S[4,5]  0.478573  0.026966 17.7474 < 2.2e-16 ***
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Goodness-of-fit indices:
                                    Value
Sample size                      838.0000
Chi-square of target model       344.1826
DF of target model                40.0000
p value of target model            0.0000
Chi-square of independent model 1461.6701
DF of independent model           50.0000
RMSEA                              0.2131
SRMR                               0.1508
TLI                                0.7307
CFI                                0.7845
AIC                              264.1826
BIC                               74.9419
OpenMx status: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Extract the pooled correlation matrices
R> coef(fixed1.cluster)

$`Older participants`
           x1         x2        x3        x4         x5
x1 1.00000000 0.29748426 0.3700879 0.1376877 0.09797102
x2 0.29748426 1.00000000 0.3937095 0.1829840 0.09266441
x3 0.37008785 0.39370949 1.0000000 0.2607561 0.09606280
x4 0.13768766 0.18298404 0.2607561 1.0000000 0.41175343
x5 0.09797102 0.09266441 0.0960628 0.4117534 1.00000000

$`Younger participants`
            x1          x2        x3          x4         x5
x1  1.00000000  0.60439588 0.4654414 -0.03086891 0.06158054
x2  0.60439588  1.00000000 0.5013091 -0.06083381 0.32101905
x3  0.46544142  0.50130913 1.0000000  0.17542223 0.30521426
x4 -0.03086891 -0.06083381 0.1754222  1.00000000 0.47857275
x5  0.06158054  0.32101905 0.3052143  0.47857275 1.00000000

R> fixed2.cluster <- tssem2(fixed1.cluster, Amatrix=A1, Smatrix=S1, Fmatrix=F1,
                            diag.constraints=TRUE, intervals.type="LB")
```

```
Running TSSEM2 (Fixed Effects Model) Analysis of Correlation Structure
Running TSSEM2 (Fixed Effects Model) Analysis of Correlation Structure

R> summary(fixed2.cluster)

$`Older participants`

Call:
wls(Cov = tssem1.obj$pooledS, asyCov = tssem1.obj$acovS, n = tssem1.obj$total.n,
    Amatrix = Amatrix, Smatrix = Smatrix, Fmatrix = Fmatrix,
    diag.constraints = diag.constraints, cor.analysis = cor.analysis,
    intervals.type = intervals.type, model.name = model.name,
    suppressWarnings = suppressWarnings)

95% confidence intervals: Likelihood-based statistic
Coefficients:
             Estimate Std.Error  lbound  ubound z value
Amatrix[1,7]  0.48671        NA 0.44908 0.52432      NA
Amatrix[2,6]  0.52460        NA 0.49543 0.55387      NA
Amatrix[3,6]  0.65180        NA 0.62355 0.68029      NA
Amatrix[4,6]  0.63182        NA 0.60170 0.66210      NA
Amatrix[5,7]  0.47139        NA 0.43253 0.51019      NA
Smatrix[1,1]  0.76312        NA 0.72509 0.79832      NA
Smatrix[2,2]  0.72479        NA 0.69323 0.75455      NA
Smatrix[3,3]  0.57516        NA 0.53720 0.61119      NA
Smatrix[4,4]  0.60080        NA 0.56162 0.63796      NA
Smatrix[5,5]  0.77779        NA 0.73970 0.81292      NA
Smatrix[7,6]  0.99100        NA 0.93156 1.05849      NA
             Pr(>|z|)
Amatrix[1,7]       NA
Amatrix[2,6]       NA
Amatrix[3,6]       NA
Amatrix[4,6]       NA
Amatrix[5,7]       NA
Smatrix[1,1]       NA
Smatrix[2,2]       NA
Smatrix[3,3]       NA
Smatrix[4,4]       NA
Smatrix[5,5]       NA
Smatrix[7,6]       NA

Goodness-of-fit indices:
                                               Value
Sample size                                3658.0000
Chi-square of target model                  510.6333
DF of target model                            4.0000
p value of target model                       0.0000
```

```
Number of constraints imposed on "Smatrix"    5.0000
DF manually adjusted                          0.0000
Chi-square of independent model            2940.1270
DF of independent model                      10.0000
RMSEA                                         0.1861
SRMR                                          0.1334
TLI                                           0.5677
CFI                                           0.8271
AIC                                         502.6333
BIC                                         477.8146
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

$`Younger participants`

Call:
wls(Cov = tssem1.obj$pooledS, asyCov = tssem1.obj$acovS, n = tssem1.obj$total.n,
    Amatrix = Amatrix, Smatrix = Smatrix, Fmatrix = Fmatrix,
    diag.constraints = diag.constraints, cor.analysis = cor.analysis,
    intervals.type = intervals.type, model.name = model.name,
    suppressWarnings = suppressWarnings)

95% confidence intervals: Likelihood-based statistic
Coefficients:
             Estimate Std.Error  lbound  ubound z value
Amatrix[1,7]  0.52484        NA 0.47174 0.57535      NA
Amatrix[2,6]  0.78495        NA 0.74995 0.82035      NA
Amatrix[3,6]  0.66595        NA 0.62729 0.70432      NA
Amatrix[4,6]  0.45613        NA 0.40515 0.50694      NA
Amatrix[5,7]  0.59209        NA 0.53203 0.64914      NA
Smatrix[1,1]  0.72454        NA 0.66897 0.77746      NA
Smatrix[2,2]  0.38385        NA 0.32701 0.43758      NA
Smatrix[3,3]  0.55651        NA 0.50393 0.60651      NA
Smatrix[4,4]  0.79194        NA 0.74302 0.83585      NA
Smatrix[5,5]  0.64942        NA 0.57860 0.71694      NA
Smatrix[7,6]  1.36830        NA 1.27802 1.48517      NA
             Pr(>|z|)
Amatrix[1,7]       NA
Amatrix[2,6]       NA
Amatrix[3,6]       NA
Amatrix[4,6]       NA
Amatrix[5,7]       NA
Smatrix[1,1]       NA
Smatrix[2,2]       NA
Smatrix[3,3]       NA
Smatrix[4,4]       NA
Smatrix[5,5]       NA
Smatrix[7,6]       NA
```

```
Goodness-of-fit indices:
                                               Value
Sample size                                 838.0000
Chi-square of target model                  314.7823
DF of target model                            4.0000
p value of target model                       0.0000
Number of constraints imposed on "Smatrix"    5.0000
DF manually adjusted                          0.0000
Chi-square of independent model            3632.8021
DF of independent model                      10.0000
RMSEA                                         0.3047
SRMR                                          0.2347
TLI                                           0.7855
CFI                                           0.9142
AIC                                         306.7823
BIC                                         287.8582
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

3.2. Random-effects model

TSSEM using a random-effects model may be requested by specifying the `method='REM'` argument in `tssem1()`. By default (`RE.diag.only=FALSE`), a positive definite covariance matrix among the random-effects is used. For practical reasons, e.g., there are not enough studies, it may not be feasible to estimate the full covariance matrix of the random effects. A diagonal matrix on the random-effects may also be used by specifying `RE.diag.only=TRUE`. The fit indices for fitting the structural model in Stage 2 are $\chi^2(4, N = 4496) = 8.28, p < .001$, CFI=0.9920, TLI=0.9801, SRMR=0.0154 and RMSEA=0.0154. This indicates that the model fits the data quite well.

```
R> random1 <- tssem1(Digman97$data, Digman97$n, method="REM", RE.diag.only=TRUE)

Running TSSEM1 (Random Effects Model) Analysis of Correlation Matrix

R> summary(random1)

Call:
meta(y = ES, v = acovR, RE.constraints = diag(x = paste(RE.startvalues,
    "*Tau2_", 1:no.es, "_", 1:no.es, sep = ""), nrow = no.es,
    ncol = no.es), I2 = I2, model.name = model.name)

95% confidence intervals: z statistic approximation
Coefficients:
              Estimate   Std.Error      lbound      ubound
Intercept1  0.39981616  0.05455521  0.29288991  0.50674240
Intercept2  0.44433503  0.04168026  0.36264323  0.52602683
```

```
Intercept3   0.05444821  0.06316912 -0.06936099  0.17825740
Intercept4   0.10138329  0.04681343  0.00963065  0.19313593
Intercept5   0.43415295  0.04000883  0.35573708  0.51256881
Intercept6   0.12867856  0.04174106  0.04686759  0.21048953
Intercept7   0.20732505  0.04973237  0.10985139  0.30479870
Intercept8   0.24064433  0.03220608  0.17752158  0.30376708
Intercept9   0.19296080  0.04340494  0.10788867  0.27803292
Intercept10  0.44713470  0.03211662  0.38418729  0.51008211
Tau2_1_1     0.03815841  0.01523926  0.00829000  0.06802682
Tau2_2_2     0.02132562  0.00868724  0.00429894  0.03835230
Tau2_3_3     0.05115980  0.02059751  0.01078943  0.09153017
Tau2_4_4     0.02571721  0.01094038  0.00427445  0.04715996
Tau2_5_5     0.01901262  0.00820033  0.00294026  0.03508498
Tau2_6_6     0.01977637  0.00914599  0.00185056  0.03770218
Tau2_7_7     0.02995567  0.01234177  0.00576625  0.05414510
Tau2_8_8     0.01030039  0.00505944  0.00038407  0.02021671
Tau2_9_9     0.02172535  0.00934582  0.00340788  0.04004282
Tau2_10_10   0.01122090  0.00494562  0.00152766  0.02091414
            z value  Pr(>|z|)
Intercept1   7.3287 2.325e-13 ***
Intercept2  10.6606 < 2.2e-16 ***
Intercept3   0.8619  0.388719
Intercept4   2.1657  0.030335 *
Intercept5  10.8514 < 2.2e-16 ***
Intercept6   3.0828  0.002051 **
Intercept7   4.1688 3.062e-05 ***
Intercept8   7.4720 7.905e-14 ***
Intercept9   4.4456 8.765e-06 ***
Intercept10 13.9222 < 2.2e-16 ***
Tau2_1_1     2.5040  0.012281 *
Tau2_2_2     2.4548  0.014095 *
Tau2_3_3     2.4838  0.012999 *
Tau2_4_4     2.3507  0.018740 *
Tau2_5_5     2.3185  0.020421 *
Tau2_6_6     2.1623  0.030595 *
Tau2_7_7     2.4272  0.015217 *
Tau2_8_8     2.0359  0.041763 *
Tau2_9_9     2.3246  0.020093 *
Tau2_10_10   2.2689  0.023277 *
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1

Q statistic on homogeneity of effect sizes: 2694.373
Degrees of freedom of the Q statistic: 130
P value of the Q statistic: 0
Heterogeneity indices (based on the estimated Tau2):
                              Estimate
```

```
Intercept1: I2 (Q statistic)    0.9597
Intercept2: I2 (Q statistic)    0.9283
Intercept3: I2 (Q statistic)    0.9496
Intercept4: I2 (Q statistic)    0.9008
Intercept5: I2 (Q statistic)    0.9193
Intercept6: I2 (Q statistic)    0.8750
Intercept7: I2 (Q statistic)    0.9184
Intercept8: I2 (Q statistic)    0.8008
Intercept9: I2 (Q statistic)    0.8877
Intercept10: I2 (Q statistic)   0.8696

Number of studies (or clusters): 14
Number of observed statistics: 140
Number of estimated parameters: 20
Degrees of freedom: 120
-2 log likelihood: -109.6847
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ##### Extract the fixed-effects (pooled correlation matrix)
R> coef(random1, select="fixed")

 Intercept1  Intercept2  Intercept3  Intercept4  Intercept5
 0.39981616  0.44433503  0.05444821  0.10138329  0.43415295
 Intercept6  Intercept7  Intercept8  Intercept9 Intercept10
 0.12867856  0.20732505  0.24064433  0.19296080  0.44713470

R> ##### Extract the sampling variance covariance matrix
R> vcov(random1, select="fixed")

               Intercept1    Intercept2   Intercept3
Intercept1   2.971643e-03  4.882045e-05 3.569778e-05
Intercept2   4.882045e-05  1.735261e-03 4.983673e-05
Intercept3   3.569778e-05  4.983673e-05 3.988377e-03
Intercept4   3.692228e-05  2.871922e-05 1.239071e-04
Intercept5   6.644416e-05  4.542286e-05 1.547136e-05
Intercept6  -5.730980e-06  6.374690e-06 1.069199e-04
Intercept7   5.089118e-07  4.445662e-06 4.208838e-05
Intercept8   3.231296e-06 -1.405955e-05 1.208248e-04
Intercept9   6.773077e-06 -1.495886e-06 4.465584e-05
Intercept10  2.837357e-06  3.261207e-06 1.324198e-05
               Intercept4   Intercept5    Intercept6
Intercept1   3.692228e-05 6.644416e-05 -5.730980e-06
Intercept2   2.871922e-05 4.542286e-05  6.374690e-06
Intercept3   1.239071e-04 1.547136e-05  1.069199e-04
Intercept4   2.189113e-03 1.511075e-05  3.989855e-05
Intercept5   1.511075e-05 1.589619e-03  4.616246e-05
Intercept6   3.989855e-05 4.616246e-05  1.739234e-03
```

```
Intercept7   1.146084e-04 2.227720e-05  1.194529e-04
Intercept8   4.672660e-05 1.193903e-05  1.017265e-04
Intercept9   1.349447e-04 2.750647e-05  4.064882e-05
Intercept10 -7.762461e-06 3.784392e-06  3.451132e-05
              Intercept7    Intercept8    Intercept9
Intercept1  5.089118e-07  3.231296e-06  6.773077e-06
Intercept2  4.445662e-06 -1.405955e-05 -1.495886e-06
Intercept3  4.208838e-05  1.208248e-04  4.465584e-05
Intercept4  1.146084e-04  4.672660e-05  1.349447e-04
Intercept5  2.227720e-05  1.193903e-05  2.750647e-05
Intercept6  1.194529e-04  1.017265e-04  4.064882e-05
Intercept7  2.471763e-03  3.805730e-05  1.056961e-04
Intercept8  3.805730e-05  1.032978e-03  1.102280e-04
Intercept9  1.056961e-04  1.102280e-04  1.882443e-03
Intercept10 1.192793e-05  1.889368e-05  3.490300e-05
              Intercept10
Intercept1   2.837357e-06
Intercept2   3.261207e-06
Intercept3   1.324198e-05
Intercept4  -7.762461e-06
Intercept5   3.784392e-06
Intercept6   3.451132e-05
Intercept7   1.192793e-05
Intercept8   1.889368e-05
Intercept9   3.490300e-05
Intercept10  1.023027e-03

R> ##### Extract the random-effects (variance component)
R> coef(random1, select="random")

  Tau2_1_1   Tau2_2_2   Tau2_3_3   Tau2_4_4   Tau2_5_5
0.03815841 0.02132562 0.05115980 0.02571721 0.01901262
  Tau2_6_6   Tau2_7_7   Tau2_8_8   Tau2_9_9 Tau2_10_10
0.01977637 0.02995567 0.01030039 0.02172535 0.01122090

R> random2 <- tssem2(random1, Amatrix=A1, Smatrix=S1, Fmatrix=F1, diag.constraints=TRUE, i

Running TSSEM2 (Random Effects Model) Analysis of Correlation Structure

R> summary(random2)

Call:
wls(Cov = pooledS, asyCov = asyCov, n = tssem1.obj$total.n, Amatrix = Amatrix,
    Smatrix = Smatrix, Fmatrix = Fmatrix, diag.constraints = diag.constraints,
    cor.analysis = cor.analysis, intervals.type = intervals.type,
    model.name = model.name, suppressWarnings = suppressWarnings)
```

```
95% confidence intervals: Likelihood-based statistic
Coefficients:
             Estimate Std.Error  lbound  ubound z value
Amatrix[1,7]  0.36594        NA 0.19372 0.49145      NA
Amatrix[2,6]  0.52776        NA 0.44394 0.61420      NA
Amatrix[3,6]  0.58872        NA 0.50989 0.67281      NA
Amatrix[4,6]  0.48963        NA 0.41993 0.56199      NA
Amatrix[5,7]  0.34919        NA 0.18457 0.46998      NA
Smatrix[1,1]  0.86609        NA 0.75848 0.96235      NA
Smatrix[2,2]  0.72147        NA 0.62274 0.80291      NA
Smatrix[3,3]  0.65341        NA 0.54730 0.74001      NA
Smatrix[4,4]  0.76026        NA 0.68417 0.82366      NA
Smatrix[5,5]  0.87806        NA 0.77913 0.96583      NA
Smatrix[7,6]  1.76399        NA 1.30134 3.49213      NA
             Pr(>|z|)
Amatrix[1,7]       NA
Amatrix[2,6]       NA
Amatrix[3,6]       NA
Amatrix[4,6]       NA
Amatrix[5,7]       NA
Smatrix[1,1]       NA
Smatrix[2,2]       NA
Smatrix[3,3]       NA
Smatrix[4,4]       NA
Smatrix[5,5]       NA
Smatrix[7,6]       NA

Goodness-of-fit indices:
                                               Value
Sample size                                4496.0000
Chi-square of target model                   81.2723
DF of target model                            4.0000
p value of target model                       0.0000
Number of constraints imposed on "Smatrix"    5.0000
DF manually adjusted                          0.0000
Chi-square of independent model             546.8082
DF of independent model                      10.0000
RMSEA                                         0.0656
SRMR                                          0.1323
TLI                                           0.6401
CFI                                           0.8561
AIC                                          73.2723
BIC                                          47.6285
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

4. Other Useful Functions

4.1. Analysis of Correlation/Covariance Structure with Weighted Least Squares

The `wls()` function may be used to fit a correlation/covariance structure with weighted least squares (WLS) estimation method. The following example fits a one-factor CFA model on the correlation matrix with WLS estimation method. It should be noted that the only off-diagonal elements are used when a correlation structure is fitted.

```
R> #### Analysis of correlation structure
R> R1 <- matrix(c(1.00, 0.22, 0.24, 0.18,
                 0.22, 1.00, 0.30, 0.22,
                 0.24, 0.30, 1.00, 0.24,
                 0.18, 0.22, 0.24, 1.00), ncol=4, nrow=4)
R> n <- 1000
R> acovR1 <- asyCov(R1, n)
R> ## One-factor CFA model
R> (A1 <- cbind(matrix(0, nrow=5, ncol=4),
               matrix(c("0.2*a1","0.2*a2","0.2*a3","0.2*a4",0),
               ncol=1)))

     [,1] [,2] [,3] [,4] [,5]
[1,] "0"  "0"  "0"  "0"  "0.2*a1"
[2,] "0"  "0"  "0"  "0"  "0.2*a2"
[3,] "0"  "0"  "0"  "0"  "0.2*a3"
[4,] "0"  "0"  "0"  "0"  "0.2*a4"
[5,] "0"  "0"  "0"  "0"  "0"

R> A1 <- as.mxMatrix(A1)
R> (S1 <- diag(c("0.2*e1","0.2*e2","0.2*e3","0.2*e4",1)))

     [,1]     [,2]     [,3]     [,4]     [,5]
[1,] "0.2*e1" "0"      "0"      "0"      "0"
[2,] "0"      "0.2*e2" "0"      "0"      "0"
[3,] "0"      "0"      "0.2*e3" "0"      "0"
[4,] "0"      "0"      "0"      "0.2*e4" "0"
[5,] "0"      "0"      "0"      "0"      "1"

R> S1 <- as.mxMatrix(S1)
R> ## The first 4 variables are observed while the last one is latent.
R> (F1 <- create.Fmatrix(c(1,1,1,1,0), name="F1"))

FullMatrix 'F1'

@labels: No labels assigned.
```

```
@values
     [,1] [,2] [,3] [,4] [,5]
[1,]    1    0    0    0    0
[2,]    0    1    0    0    0
[3,]    0    0    1    0    0
[4,]    0    0    0    1    0

@free: No free parameters.

@lbound: No lower bounds assigned.

@ubound: No upper bounds assigned.

R> wls.fit1 <- wls(Cov=R1, asyCov=acovR1, n=n, Fmatrix=F1, Smatrix=S1, Amatrix=A1,
                   cor.analysis=TRUE, diag.constraints=TRUE, intervals="LB")

Running WLS Analysis of Correlation Structure

R> summary(wls.fit1)

Call:
wls(Cov = R1, asyCov = acovR1, n = n, Amatrix = A1, Smatrix = S1,
    Fmatrix = F1, diag.constraints = TRUE, cor.analysis = TRUE,
    intervals.type = "LB")

95% confidence intervals: Likelihood-based statistic
Coefficients:
             Estimate Std.Error  lbound  ubound z value
Amatrix[1,5]  0.42159        NA 0.34632 0.49869      NA
Amatrix[2,5]  0.52376        NA 0.44829 0.60309      NA
Amatrix[3,5]  0.57092        NA 0.49431 0.65292      NA
Amatrix[4,5]  0.42159        NA 0.34632 0.49869      NA
Smatrix[1,1]  0.82226        NA 0.75131 0.88005      NA
Smatrix[2,2]  0.72567        NA 0.63627 0.79903      NA
Smatrix[3,3]  0.67405        NA 0.57367 0.75566      NA
Smatrix[4,4]  0.82226        NA 0.75131 0.88006      NA
             Pr(>|z|)
Amatrix[1,5]       NA
Amatrix[2,5]       NA
Amatrix[3,5]       NA
Amatrix[4,5]       NA
Smatrix[1,1]       NA
Smatrix[2,2]       NA
Smatrix[3,3]       NA
Smatrix[4,4]       NA
```

```
Goodness-of-fit indices:
                                                Value
Sample size                                 1000.0000
Chi-square of target model                     0.0134
DF of target model                             2.0000
p value of target model                        0.9933
Number of constraints imposed on "Smatrix"     4.0000
DF manually adjusted                           0.0000
Chi-square of independent model              243.9826
DF of independent model                        6.0000
RMSEA                                          0.0000
SRMR                                           0.0012
TLI                                            1.0250
CFI                                            1.0000
AIC                                           -3.9866
BIC                                          -13.8021
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Extract the parameter estimates
R> coef(wls.fit1)

Amatrix[1,5] Amatrix[2,5] Amatrix[3,5] Amatrix[4,5]
   0.4215923    0.5237644    0.5709210    0.4215923
Smatrix[1,1] Smatrix[2,2] Smatrix[3,3] Smatrix[4,4]
   0.8222599    0.7256709    0.6740492    0.8222599

R> ## Extract the sampling variance covariance matrix
R> vcov(wls.fit1)

[1] NA
```

4.2. Likelihood-based Confidence Intervals

Most CIs are based on the estimated standard errors. These are known as Wald CIs. Wald CIs are symmetric around the estimates. The Wald CIs might be outside of the meaningful boundaries, for example, a negative lower limit for the variance or larger than 1 for a correlation coefficient. A preferable approach is to construct the CIs based on the likelihood. This is known as the likelihood based CI (Cheung 2009a; Neale and Miller 1997). Likelihood based CIs on the parameter estimates can be required by specifying `intervals.type='LB'` argument.

```
R> ## Random-effects meta-analysis with ML
R> summary( meta(y=di, v=vi, data=Becker83, intervals.type="LB") )

Running Meta analysis with ML
```

```
Call:
meta(y = di, v = vi, data = Becker83, intervals.type = "LB")

95% confidence intervals: Likelihood-based statistic
Coefficients:
            Estimate Std.Error    lbound    ubound z value
Intercept1  0.174734  0.113378 -0.052165  0.437627  1.5412
Tau2_1_1    0.077376  0.054108  0.015124  0.302999  1.4300
           Pr(>|z|)
Intercept1   0.1233
Tau2_1_1     0.1527

Q statistic on homogeneity of effect sizes: 30.64949
Degrees of freedom of the Q statistic: 9
P value of the Q statistic: 0.0003399239
Heterogeneity indices (I2) and their 95% likelihood-based CIs:
                              lbound Estimate ubound
Intercept1: I2 (Q statistic) 0.28410  0.67182 0.8888

Number of studies (or clusters): 10
Number of observed statistics: 10
Number of estimated parameters: 2
Degrees of freedom: 8
-2 log likelihood: 7.928307
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)

R> ## Mixed-effects meta-analysis with "log(items)" as a predictor
R> summary( meta(y=di, v=vi, x=log(items), data=Becker83, intervals.type="LB") )

Running Meta analysis with ML

Call:
meta(y = di, v = vi, x = log(items), data = Becker83, intervals.type = "LB")

95% confidence intervals: Likelihood-based statistic
Coefficients:
              Estimate   Std.Error      lbound      ubound
Intercept1 -3.2015e-01  1.0981e-01 -5.4408e-01 -7.7598e-02
Slope1_1    2.1088e-01  4.5084e-02  1.1838e-01  3.0789e-01
Tau2_1_1    1.0000e-10  2.0095e-02  9.9937e-11  5.7947e-02
           z value  Pr(>|z|)
Intercept1 -2.9154  0.003552 **
Slope1_1    4.6774 2.905e-06 ***
Tau2_1_1    0.0000  1.000000
---
Signif. codes:  0 ‘***’ 0.001 ‘**’ 0.01 ‘*’ 0.05 ‘.’ 0.1 ‘ ’ 1
```

```
Q statistic on homogeneity of effect sizes: 30.64949
Degrees of freedom of the Q statistic: 9
P value of the Q statistic: 0.0003399239
Explained variances (R2):
                            Estimate
y1: Tau2 (no predictor)       0.0774
y1: Tau2 (with predictors)    0.0000
y1: R2                        1.0000

Number of studies (or clusters): 10
Number of observed statistics: 10
Number of estimated parameters: 3
Degrees of freedom: 7
-2 log likelihood: -4.208024
OpenMx status1: 0 ("0" and "1": considered fine; other values indicate problems)
```

4.3. Reading External Data Files

Data sets are most likely stored externally. metaSEM reads three types of data formats. The first type is full correlation/covariance matrices, for example, fullmat.dat is the same as the built-in data set Cheung09. Missing values are represented by NA (the default option). Suppose you have saved it at d:\fullmat.dat, you may read it by using the following command in R:

```
my.df <- readFullMat(file="d:/fullmat.dat")
```

The second type is lower triangle correlation/covariance matrices, for example, lowertriangle.dat. Missing values are represented by the strings NA. Suppose you have saved it at d:\lowertriangle.dat, you may read it by using the following command in R:

```
my.df <- readLowTriMat(file = "d:/lowertriangle.dat", no.var = 9, na.strings="NA")
```

The third type is vectors of correlation/covariance elements based on column vectorization. One row represents one study, for example, stackvec.dat. Suppose you have saved it at d:\stackvec.dat, you may read it by using the following R command:

```
my.df <- readStackVec(file="d:/stackvec.dat")
```

5. Installation

First of all, you need R to run it. Since metaSEM uses OpenMx as the workhorse, OpenMx has to be installed first. To install OpenMx, run the following command inside an R session:

```
install.packages('OpenMx', repos='http://openmx.psyc.virginia.edu/packages/')
```

See http://openmx.psyc.virginia.edu/installing-openmx for the details on how to install OpenMx. Moreover, metaSEM also depends on the ellipse package that can be installed by the following command inside an R session:

```
install.packages('ellipse')
```

5.1. Windows platform

Download the Windows binary of metaSEM. If the file is saved at d:\. Run the following command inside an R session:

```
install.packages(pkgs="d:/metaSEM_0.7-1.zip", repos=NULL)
```

Please note that d:\ in Windows is represented by either d:/ or d:\\ in R.

5.2. Linux and Mac OS X platform

Download the source package of metaSEM. Run the following command (as Root) inside an R session:

```
install.packages(pkgs="metaSEM_0.7-1.zip", repos=NULL, type="source")
```

6. Acknowledgements

This package cannot be written without R and OpenMx. Contributions by the R Development Core Team and the OpenMx Core Development Team are highly appreciated.

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Affiliation:

Mike W.-L. Cheung
Department of Psychology
Faculty of Arts and Social Sciences
National University of Singapore
Singapore 117570
E-mail: mikewlcheung@nus.edu.sg
URL: http://courses.nus.edu.sg/course/psycwlm/internet/metaSEM/