Fitting Flexible Meta-Analytic Models with Structural Equation Modeling

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Overview of main functions in metaSEM package

- The metaSEM[1] package uses the OpenMx[2] and lavaan[3] packages to conduct meta-analysis, and the semPlot package[4] for visualizaiton.
- Calculating effect sizes and their sampling covariance matrices
  - asyCov(), calEffSizes(), smdMES(), and smdMTS().
- Meta-analytic structural equation modeling (MASEM)
  - Two-stage SEM (with Wai Chan): tssem1(), tssem2(), and wls().
  - One-stage MASEM (with Suzanne Jak): osmasem() for correlation matrices and osmasem2() for covariance/correlation matrices and means (new!).
- SEM-based meta-analysis
  - Univariate and multivariate meta-analyses: meta() and metaFIML().
  - Three-level meta-analysis: meta3L() and meta3LFIML().
  - Fitting flexible models: sem() (today's talk).

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[1] Cheung, M. W.-L. (2015). metaSEM: An R package for meta-analysis using structural equation modeling. *Frontiers in Psychology*, *5*(1521). https://doi.org/10.3389/fpsyg.2014.01521

[2] Boker, S., Neale, M., Maes, H., Wilde, M., Spiegel, M., Brick, T., Spies, J., Estabrook, R., Kenny, S., Bates, T., Mehta, P., & Fox, J. (2011). OpenMx: An open source extended structural equation modeling framework. *Psychometrika*, *76*(2), 306–317. https://doi.org/10.1007/s11336-010-9200-6

[3] Rosseel, Y. (2012). lavaan: An R package for structural equation modeling. *Journal of Statistical Software*, *48*(2), 1–36.

[4] Epskamp, S. (2015). semPlot: Unified Visualizations of Structural Equation Models. *Structural Equation Modeling: A Multidisciplinary Journal*, *22*(3), 474–483

Introduction

- Researchers usually learn meta-analytic models by comprehending the mathematics and algorithms.
- They often need to wait for programs, such as the `metafor`[5] package in `R`, to implement these models.
- Customizing meta-analytic models can be challenging, for example, fitting regression or mediation models with effect sizes.
- This talk introduces an SEM approach to address these concerns.

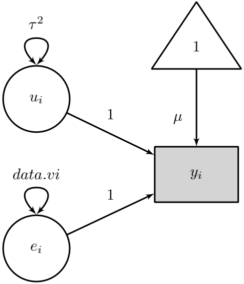
[5] Viechtbauer, W. (2010). Conducting meta-analyses in R with the metafor package. *Journal of Statistical Software*, *36*(3), 1–48. https://doi.org/10.18637/jss.v036.i03

A random-effects model with additive heterogeneity

- $y_i = \mu + u_i + e_i$, with $\mathrm{E}(y_i) = \mu$, $\mathrm{Var}(e_i) = v_i$, and $\mathrm{Var}(u_i) = \tau^2$.
- A fixed- (or common-) effect model is a special case when $\tau^2 = 0$.
- SEM notations:

- $\square$: an observed variable
- $\bigcirc$: a latent variable
- $\triangle$: a mean or intercept
- $\rightarrow$: prediction or "cause," e.g., a regression coefficient
- $\leftrightarrow$: association, e.g., a covariance or variance
- *data.vi*: assigning v_i to the parameter (only in OpenMx)

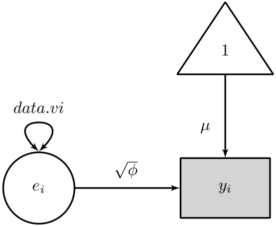
- Mean structure: $\mu_i(\theta) = \mu$.
- Variance structure: $\Sigma_i(\theta) = \tau^2 + v_i$.



A model with multiplicative heterogeneity

- The random-effects model with additive error is not the only model in the literature.
- There are debates whether the heterogeneity should be additive or multiplicative.[6], [7]
- $y_i = \mu + \sqrt{\phi} e_i$, with $\mathrm{E}(y_i) = \mu$ and $\mathrm{Var}(e_i) = v_i$.
- ϕ is the scaling factor of the multiplicative heterogeneity variance.

- Mean structure: $\mu_i(\theta) = \mu$.
- Variance structure: $\Sigma_i(\theta) = \phi v_i$.



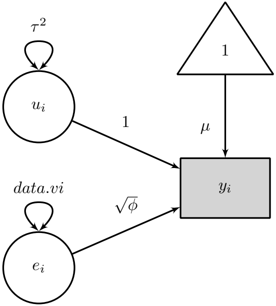
[6] Mawdsley, D., Higgins, J. P. T., Sutton, A. J., & Abrams, K. R. (2017). Accounting for heterogeneity in meta-analysis using a multiplicative model—An empirical study. *Research Synthesis Methods*, *8*(1), 43–52. https://doi.org/10.1002/jrsm.1216

[7] Stanley, T. D., & Doucouliagos, H. (2015). Neither fixed nor random: Weighted least squares meta-analysis. *Statistics in Medicine*, *34*(13), 2116–2127. https://doi.org/10.1002/sim.6481

Additive or multiplicative or both?

- A hybrid model including both addictive and multiplicative heterogeneity has been proposed.[8], [9]

- Mean structure: $\mu_i(\theta) = \mu$.
- Variance structure: $\Sigma_i(\theta) = \tau^2 + \phi v_i$.

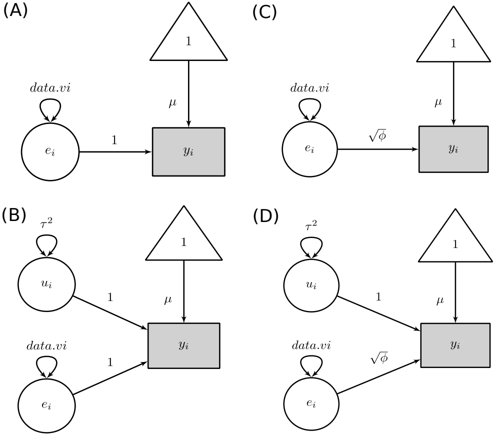


[8] Baker, R. D., & Jackson, D. (2013). Meta-analysis inside and outside particle physics: Two traditions that should converge? *Research Synthesis Methods*, *4*(2), 109–124. https://doi.org/10.1002/jrsm.1065

[9] Schmid, C. H. (2017). Heterogeneity: Multiplicative, additive or both? *Research Synthesis Methods*, *8*(1), 119–120. https://doi.org/10.1002/jrsm.1223

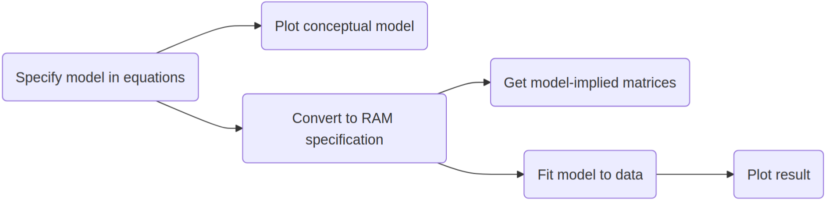
Comparison of the above models

- Some of them are nested.
- AIC and BIC have been utilized for model comparison,[10] but it is unclear whether this is the best approach.



[10] Stanley, T. D., Ioannidis, J. P. A., Maier, M., Doucouliagos, H., Otte, W. M., & Bartoš, F. (2023). Unrestricted weighted least squares represent medical research better than random effects in 67,308 Cochrane meta-analyses. *Journal of Clinical Epidemiology*, *157*, 53–58.

Typical workflow



Example 1: A hybrid model with both additive and multiplicate heterogeneity[11]

- Effect size (correlation between organizational commitment and salesperson job performance): *yi*.
- Sampling variance: *vi*.
- Covariate (Individualism scores of the studies): *xi*

[11] Jaramillo, F., Mulki, J. P., & Marshall, G. W. (2005). A meta-analysis of the relationship between organizational commitment and salesperson job performance: 25 years of research. *Journal of Business Research*, *58*(6), 705–714. https://doi.org/10.1016/j.jbusres.2003.10.004

Step 0: Load the libraries and prepare the data

```
library(metaSEM)
library(symSEM)   ## To calculate the model-implied matrices

## Prepare the data for demonstration
dat <- data.frame(yi=Jaramillo05$r,
                  vi=Jaramillo05$r_v,
                  ## Center, but not scale, the covariate
                  xi=scale(Jaramillo05$IDV, scale=FALSE))
head(dat)
```

```
##     yi          vi         xi
## 1 0.02 0.005582124 -33.836066
## 2 0.12 0.004187101   9.163934
## 3 0.09 0.001756903   9.163934
## 4 0.20 0.005091713 -14.836066
## 5 0.08 0.006328468   9.163934
## 6 0.04 0.005537792   9.163934
```

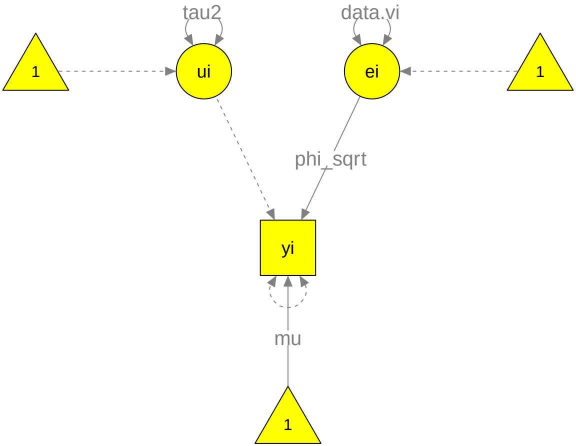
Step 1: Specify the model in R

- Readers may refer to the lavaan website for the lavaan syntax to specify structural equation models.

```
## Specify a hybrid model and call it "m1"
m1 <- "yi ~ mu*1            ## Mean(yi) = mu
       yi ~~ 0*yi           ## Measurement error is fixed at 0
       ## Additive error
       ui =~ 1*yi           ## yi = 1*ui
       ui ~~ tau2*ui        ## Var(ui) = tau2
       ## Multiplicative error
       ei =~ phi_sqrt*yi    ## yi = phi_sqrt*ei
       ei ~~ data.vi*ei     ## Var(ei) = vi
       phi := phi_sqrt^2    ## Define phi as a function of
                            ## (phi_sqrt)^2
"
```

Step 2: Plot the conceptual model (optional)

```
plot(m1, color="yellow", sizeInt=7)
```



Step 3: Symbolically derive the model implied mean and variance structures (optional)

```
## Convert the model to a RAM specification
ram1 <- lavaan2RAM(m1, obs.variables = "yi", std.lv = FALSE)

## Get the model implied structures
impliedS(ram1)
```

```
## Model implied covariance matrix (Sigma):
```

```
##    yi
## yi "data.vi*phi_sqrt^2 + tau2"
```

```
## Model implied mean vector (Mu):
```

```
##   yi
## 1 "mu"
```

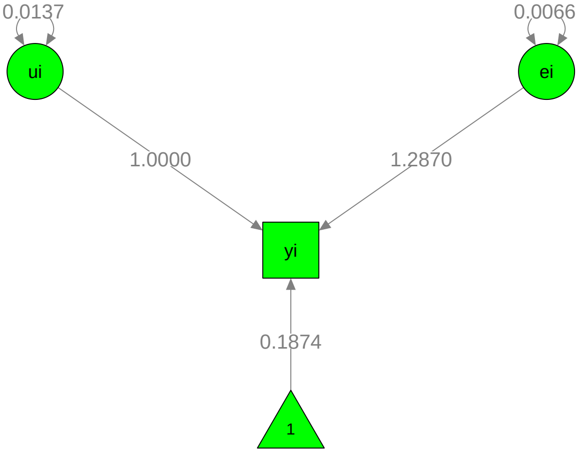
Step 4: Fit the model with data

```
## Use the likelihood-based CI for phi=phi_sqrt^2
hybrid <- sem("Hybrid", RAM=ram1, data=dat, intervals.type="LB")
summary(hybrid)
```

```
## 95% confidence intervals: Likelihood-based statistic
## Coefficients:
##           Estimate Std.Error     lbound     ubound z value Pr(>|z|)
## mu       0.1873704        NA  0.1488124  0.2257397      NA       NA
## phi_sqrt  1.2870404        NA -2.0902766  2.0872970      NA       NA
## tau2     0.0136638        NA  0.0039765  0.0304225      NA       NA
##
## Mxalgebras:
##          lbound estimate   ubound
## phi 1.805558e-44 1.656473 4.361042
##
## Information Criteria:
##      df Penalty Parameters Penalty Sample-Size Adjusted
## AIC:  -171.7740          -49.77403            -49.35298
## BIC:  -294.2047          -43.44141            -52.87879
##
## Number of subjects (or studies): 61
## Number of observed statistics: 61
## Number of estimated parameters: 3
## Degrees of freedom: 58
## -2 log likelihood: -55.77403
## OpenMx status1: 0 ("0" or "1": The optimization is considered fine.
## Other values may indicate problems.)
```

Step 5: Plot the model with the parameter estimates (optional)

```
plot(hybrid, color="green", sizeInt=7, nDigits=4)
```



Let's compare all four models

- The hybrid model has the lowest AIC (best model), while the random-effects model's AIC is also very similar.
- The fixed-effect model has the largest AIC (worst model).

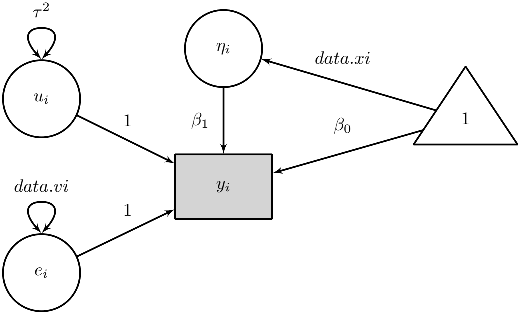
```
anova(hybrid, random, multi, fixed)
```

```
##     base     comparison ep  minus2LL df       AIC     diffLL
## 1 Hybrid           <NA>  3 -55.77403 58 -49.77403         NA
## 2 Hybrid         Random  2 -53.28211 59 -49.28211   2.491919
## 3 Hybrid Multiplicative  2 -44.62625 59 -40.62625  11.147781
## 4 Hybrid          Fixed  1 129.06973 60 131.06973 184.843761
##              p
## 1           NA
## 2 1.144321e-01
## 3 8.413227e-04
## 4 7.272559e-41
```

A mixed-effects model with a predictor x_i as a design matrix

- In a mixed-effects meta-analysis or meta-regression, the predictors are treated as a design matrix without any distribution assumption. This is known as the fixed-x approach.
- $y_i = \beta_0 + \beta_1 x_i + u_i + e_i$.

- Mean structure: $\mu_i(\theta) = \beta_0 + \beta_1 x_i$.
- Variance structure: $\Sigma_i(\theta) = \tau^2 + data.vi$.



A mixed-effects model with a predictor x_i as a variable

- In SEM, the predictors are usually treated as variables. This is known as the random-x approach.
- Pros: handling missing predictors with FIML estimation under the assumption of missing at random (MAR).
- Cons: predictors are assumed multivariate normal.
- $y_i = \beta_0 + \beta_1 x_i + u_i + e_i$, with $\mathrm{E}(x_i) = \mu_x$, and $\mathrm{Var}(x_i) = \sigma_x^2$.

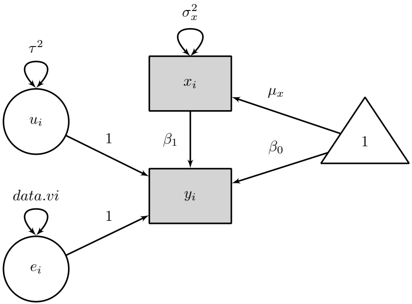
- Mean structure:

$$\mu_i(\theta) = \begin{matrix} y \\ x \end{matrix} \begin{bmatrix} \beta_0 + \beta_1 \mu_x \\ \mu_x \end{bmatrix}.$$

- Variance structure: $\Sigma_i(\theta) =$

$$\begin{matrix} & y & x \\ \begin{matrix} y \\ x \end{matrix} & \begin{bmatrix} \beta_1^2 \sigma_x^2 + \tau^2 + data.vi & \\ \beta_1 \sigma_x^2 & \sigma_x^2 \end{bmatrix} \end{matrix}.$$

- Explained variance: $R^2 = \beta_1^2 \sigma_x^2 / (\beta_1^2 \sigma_x^2 + \tau^2)$



Using true effect size as a predictor (1)

- Effect sizes may be used as predictors rather than as outcome variables:
  - An effect size predicts another variable, e.g., $z_{citations} = \beta_0 + \beta_1 y_i + e_i$[12]
  - An effect size predicts another effect size, e.g., $y_{\text{treatment benefit}} = \beta_0 + \beta_1 y_{\text{baseline risk}} + e_i$[13] and $y_{\text{debunking effect}} = \beta_0 + \beta_1 y_{\text{misinformation effect}} + e_i$ in science-relevant misinformation[14]
- The estimated regression coefficients $\hat{\beta}_1$s are biased towards zero if we use the observed effect sizes as predictors.

[12] Lortie, C. J., Aarssen, L. W., Budden, A. E., & Leimu, R. (2013). Do citations and impact factors relate to the real numbers in publications? A case study of citation rates, impact, and effect sizes in ecology and evolutionary biology. *Scientometrics*, *94*(2), 675–682. https://doi.org/10.1007/s11192-012-0822-6

[13] Arends, L. R., Hoes, A. W., Lubsen, J., Grobbee, D. E., & Stijnen, T. (2000). Baseline risk as predictor of treatment benefit: Three clinical meta-re-analyses. *Statistics in Medicine*, *19*(24), 3497–3518. https://doi.org/10.1002/1097-0258(20001230)19:24<3497::AID-SIM830>3.0.CO;2-H

[14] Chan, M. S., & Albarracín, D. (2023). A meta-analysis of correction effects in science-relevant misinformation. *Nature Human Behaviour*, *7*(9), 1514–1525. https://doi.org/10.1038/s41562-023-01623-8

Using true effect size as a predictor (2)

- f_i is the "true" effect size without sampling error:
  - $y_i = f_i + e_i$, with $\mathrm{E}(f_i) = \mu_y$ and $\mathrm{Var}(f_i) = \tau_y^2$.
- An outcome variable:
  - $z_i = \beta_0 + \beta_1 f_i + e_{zi}$, with $\mathrm{Var}(e_{zi}) = \sigma_{e_z}^2$.

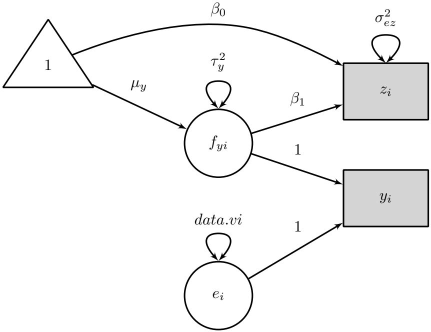
- Mean structure:

$$\mu_i(\theta) = \begin{matrix} y \\ z \end{matrix} \begin{bmatrix} \mu_y \\ \beta_0 + \beta_1 \mu_y \end{bmatrix}.$$

- Variance structure: $\Sigma_i(\theta) =$

$$\begin{matrix} & y & z \\ y & \tau_y^2 + data.vi & \\ z & \beta_1 \tau_y^2 & \beta_1^2 \tau_y^2 + \sigma_{e_z}^2 \end{matrix}.$$

- Explained variance: $\beta_1^2 \tau_y^2 / (\beta_1^2 \tau_y^2 + \sigma_{e_z}^2)$.



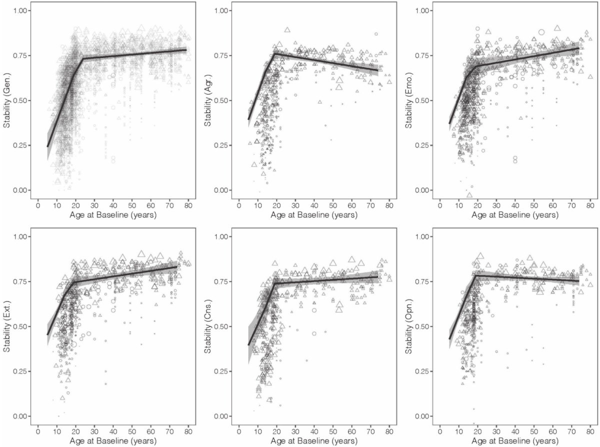
Meta-analysis beyond the linear relationship

- It is typically assumed that there is a linear relationship between the effect size and covariates.
- Additionally, it is usually assumed that the heterogeneity variance (τ^2) remains constant across different levels of the covariates.
- However, it is crucial to acknowledge that there are situations where one or both of these assumptions may not hold true.

An example of nonlinear mean structure[15]

Figure 2

Life Span Trends for Rank-Order Stability Estimates (r) for All Traits and the Big Five Separately



Note. The first panel plots results for the full data set, and the subsequent panels plot results for Extraversion, Agreeableness, Conscientiousness, Emotional Stability, and Openness, in that order. Effect sizes are plotted in addition to the best-fitting spline model and scaled relative to the weight the effect size carried in the analysis, with larger plotting characters carrying more weight. Effect sizes represented as a circle are from previous meta-analyses, and effect sizes represented as a triangle are from the newly coded data. Shading around the trend line reflects the 95% confidence interval. Gen. = general personality effect size; Ext. = Extraversion; Agr. = Agreeableness; Cns. = Conscientiousness; Emo. = Emotional Stability; Opn. = Openness.

[15] Bleidorn, W., Schwaba, T., Zheng, A., Hopwood, C. J., Sosa, S. S., Roberts, B. W., & Briley, D. A. (2022). Personality stability and change: A meta-analysis of longitudinal studies. *Psychological Bulletin*, *148*(7–8), 588–619. https://doi.org/10.1037/bul0000365

An example of non-constant heterogeneity variance[16]

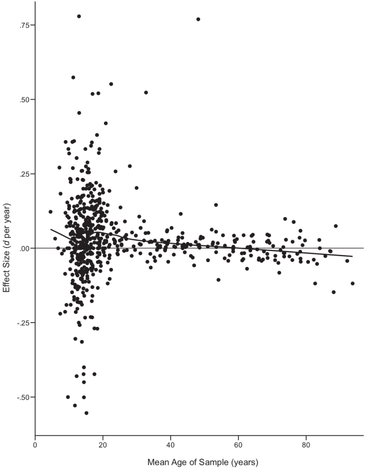


Figure 2. Scatterplot displaying the relation between effect size (i.e., standardized mean change *d* per year, d_{year}) and age (i.e., mean age of sample at the center of the observed time interval). The figure also shows the locally weighted smoothing (LOESS) curve across age.

[16] Orth, U., Erol, R. Y., & Luciano, E. C. (2018). Development of self-esteem from age 4 to 94 years: A meta-analysis of longitudinal studies. *Psychological Bulletin*, *144*(10), 1045–1080. https://doi.org/10.1037/bul0000161

Example 2: Location-scale[17] and nonlinear models

- A location-scale model:
  - $y_i = \underbrace{\mu_i}_{\text{Mean structure}} + \underbrace{u_i + e_i}_{\text{Variance structure}}.$
  - Mean structure: $\mu_i(\theta) = \mu_i = \beta_0 + \beta_1 x_i$.
  - Variance structure: $\Sigma_i(\theta) = \mathrm{Var}(u_i + e_i) = \exp(\alpha_0 + \alpha_1 x_i) + v_i$, where $\exp(\alpha_0)$ is the heterogeneity variance when $x_i = 0$.
- Notes:
  - The predictors in the mean and variance structures can be different.
  - A nonlinear structure may also be applied on the mean structure.

[17] Viechtbauer, W., & López-López, J. A. (2022). Location-scale models for meta-analysis. *Research Synthesis Methods*, *13*(6), 697–715. https://doi.org/10.1002/jrsm.1562

Step 1: Specify a location-scale model with 6 lines of R code

- We may fit arbitrary structures with the == operator:
  - `mu == b0 + b1*data.xi`
  - `tau2 == exp(a0 + a1*data.xi)`

```
m2 <- "yi ~ mu*1          ## Mean(yi) = mu
      yi ~~ data.vi*yi   ## Var(ei) = vi
      ## ui is latent variable of random effect
      ui =~ 1*yi         ## yi = 1*ui
      ui ~~ tau2*ui      ## Var(ui) = tau2
      ## Specify nonlinear models on mu and tau2
      mu == b0 + b1*data.xi
      tau2 == exp(a0 + a1*data.xi)"
```

Step 2: Symbolically derive the model implied structures

```r
## Convert the model to a RAM specification
ram2 <- lavaan2RAM(m2, obs.variables="yi", std.lv=FALSE)

## Get the model implied structures
## We need to replace the constraints with the new parameters
impliedS(ram2, replace.constraints=TRUE)
```

```
## Model implied covariance matrix (Sigma):

##    yi
## yi "data.vi + exp(a0 + a1*data.xi)"

## Model implied mean vector (Mu):

##   yi
## 1 "b0 + b1*data.xi"
```

Step 3: Fit the model with data

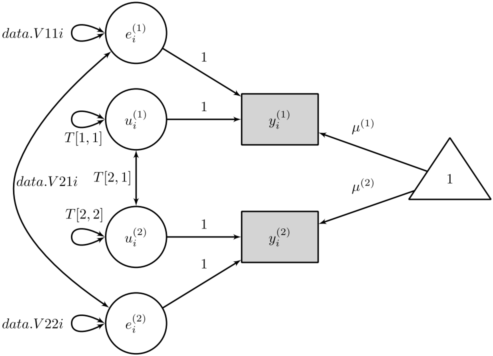
```r
## We need to replace the constraints with the new parameters
fit2 <- sem(RAM=ram2, data=dat, replace.constraints=TRUE)
summary(fit2)
```

```
## 95% confidence intervals: z statistic approximation (robust=FALSE)
## Coefficients:
##       Estimate   Std.Error      lbound      ubound  z value Pr(>|z|)
## a0 -4.11206737  0.24483731 -4.59193967 -3.63219506 -16.7951   <2e-16 ***
## a1  0.00541492  0.01314676 -0.02035226  0.03118209   0.4119   0.6804
## b0  0.18596386  0.01908419  0.14855954  0.22336818   9.7444   <2e-16 ***
## b1 -0.00129620  0.00090683 -0.00307355  0.00048115  -1.4294   0.1529
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Information Criteria:
##      df Penalty Parameters Penalty Sample-Size Adjusted
## AIC:  -171.4105          -49.41046            -48.69617
## BIC:  -291.7303          -40.96696            -53.55013
##
## Number of subjects (or studies): 61
## Number of observed statistics: 61
## Number of estimated parameters: 4
## Degrees of freedom: 57
## -2 log likelihood: -57.41046
## OpenMx status1: 0 ("0" or "1": The optimization is considered fine.
## Other values may indicate problems.)
```

A random-effects bivariate meta-analysis

- The previous univariate models can be extended to bivariate models.
- $\boldsymbol{y}_i = \boldsymbol{\mu} + \boldsymbol{u}_i + \boldsymbol{e}_i$, with $\mathrm{E}(\boldsymbol{y}_i) = \boldsymbol{\mu}$, $\mathrm{Var}(\boldsymbol{e}_i) = \boldsymbol{V}_i$, and $\mathrm{Var}(\boldsymbol{u}_i) = \boldsymbol{T}$.

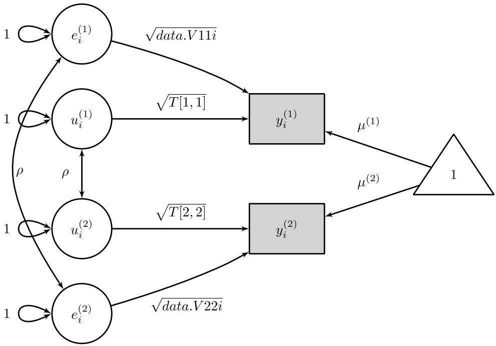
- Mean structure:
  $\boldsymbol{\mu}_i(\theta) = \begin{bmatrix} \mu^{(1)} \\ \mu^{(2)} \end{bmatrix}$.
- Variance structure:
  $\boldsymbol{\Sigma}_i(\theta) = \begin{bmatrix} T_{[1,1]} & \\ T_{[2,1]} & T_{[2,2]} \end{bmatrix} + \begin{bmatrix} V_{[1,1]i} & \\ V_{[2,1]i} & V_{[2,2]i} \end{bmatrix}$.



A random-effects bivariate meta-analysis with common between and within correlation

- One difficult aspect of applying multivariate meta-analysis is that information for calculating the sampling correlation may be missing.
- Riley et al.[18] proposed a model that assumes the between- and within-study correlations are the same.

- Mean structure: $\mu_i(\theta) = \begin{bmatrix} \mu^{(1)} \\ \mu^{(2)} \end{bmatrix}$.
- Variance structure: $\Sigma_i(\theta) = \begin{bmatrix} T_{[1,1]} & \\ \rho\sqrt{T_{[1,1]}T_{[2,2]}} & T_{[2,2]} \end{bmatrix} + \begin{bmatrix} V_{[1,1]i} & \\ \rho\sqrt{V_{[1,1]i}V_{[2,2]i}} & V_{[2,2]i} \end{bmatrix}$.



[18] Riley, R. D., Thompson, J. R., & Abrams, K. R. (2008). An alternative model for bivariate random-effects meta-analysis when the within-study correlations are unknown. *Biostatistics*, *9*(1), 172–186. https://doi.org/10.1093/biostatistics/kxm023

Strengths and limitations of the SEM-based meta-analysis

- Strengths:
  - Learning meta-analysis using graphical models
  - Deriving model-implied means and covariances
  - Fitting proposed models to data
  - Imposing linear and nonlinear constraints on the parameters
  - Creating functions of parameters and their confidence intervals, such as R^2 and indirect effect $a * b$
  - Handling missing data with the full information maximum likelihood (FIML) estimation method
  - Extending to multivariate meta-analysis and even MASEM!
- Limitations:
  - Fitting the data with FIML only
  - Using a z test rather than a t test (but easy to fix)
  - Having to implement the three-level meta-analysis and robust variance estimation (RVE).

Conclusion

- This approach can be used to fit novel meta-analytic models, which are not available in the existing meta-analysis software yet.
- The preprint is available at https://osf.io/preprints/psyarxiv/w9pc6.
- The R code for the analyses is available at https://github.com/mikewlcheung/code-in-articles/tree/master/Cheung%202024.
- Questions and comments are welcome!