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Supporting Web Materials: Programming Code for IPD Models

STATA VERSION 13

The standard fixed-effects meta-analysis (Model 16) for a dataset with variables `trial`, `treat` and `outcome` can be fitted using the Stata code

```
xi: regress outcome i.trial i.treat
```

The patient-level error can be allowed to differ by treatment, as in Model (17), using

```
xi: mixed outcome i.trial i.treat, resid(ind, by(treat))
```

The fixed-effects meta-analysis corresponding to the two-level heteroscedastic model, given in Model (18) where `t_id` is the cluster identifier, can be fitted with

```
xi: mixed outcome i.trial i.treat || t_id: treat notreat, nocons resid(ind, by(treat)) cov(independent)
```

Allowing for differences in variances is necessary so that the pooled therapist variance for each arm is correctly estimated.

For partially-nested designs, this becomes

```
xi: mixed outcome i.trial i.treat || t_id: treat, nocons resid(ind, by(treat))
```

Again for partially-nested designs, the random-effects meta-analysis, adapted from Model (18), can be fitted using

```
xi: mixed outcome i.trial i.treat || trial: treat, nocons || t_id: treat, nocons resid(ind, by(treat))
```

The meta-regression models in (22) to (25) are more intuitive to fit in MLwiN. However the Stata command for model (22) on treatment standardisation, adapted for partially nested designs, is

```
xi: mixed outcome i.trial i.treat || trial: treat, nocons || t_id: treat_stand notreat_stand treat_nonstand notreat_nonstand, nocons resid(ind, by(treat)) cov(independent)
```

where ‘`treat_stand`’, ‘`notreat_stand`’, ‘`treat_nonstand`’ and ‘`notreat_nonstand`’ are interactions of stand and not stand with treatment. The Stata command for model (23) on patient eligibility, adapted for partially nested designs, is

xi: mixed outcome i.trial i.treat || trial: treat, nocons || t_id: treat, resid(ind, by(treat_elidge))

where ‘treat_elidge’ has four categories corresponding to the combinations of treatment and eligibility.

Model (25) can be fitted by defining indicator variable ‘treatcluster’ and ‘controlcluster’ equal to 0 or 1 according to whether a patient is in a cluster in either the treatment or control arm, together with a variable with four categories, say ‘cluster’, corresponding to the four combinations of ‘treatcluster’ and ‘controlcluster’

xi: mixed outcome i.trial i.treat || trial: treatcluster controlcluster, nocons || t_id: treat, resid(ind, by(cluster))

MLwiN VERSION 2.02

A dataset was imported starting with variables study_id, t_id, p_id identifying the trial, cluster (i.e. counsellor or control patient), and patient, followed by indicator variables study_id2, study_id3, study_id6, study_id7 for Chilvers 2001, Friedli 1997, King 2000 and Simpson 2000, treatment for counselling, control for no counselling, poutcome for the BDI, and constant for a column of ones. The data were already sorted on study_id, t_id, and p_id and the data had been reduced to complete cases. Once in MLwiN, the RIGLS option under Equations was used, and the worksheet then saved. The Equations under Model was used to open an interactive window. The outcome was specified, and three levels. The standard fixed-effects meta-analysis (Model 16) was fitted as follows:

$$poutcome_{ijk} \sim N(XB, \Omega)$$

$$poutcome_{ijk} = \beta_{0i} \text{constant} + -1.288(1.402) \text{study_id3}_{jk} + -0.612(1.382) \text{study_id6}_{jk} + 0.767(1.318) \text{study_id7}_{jk} + -2.469(0.900) \text{treatment}_{jk}$$

$$\beta_{0i} = 16.148(1.139) + e_{0ijk}$$

$$\begin{bmatrix} e_{0ijk} \end{bmatrix} \sim N(0, \Omega_e) : \Omega_e = \begin{bmatrix} 92.773(6.117) \end{bmatrix}$$

$$-2 * \log \text{likelihood} (\text{IGLS Deviance}) = 3384.295 (460 \text{ of } 460 \text{ cases in use})$$

The patient-level error was allowed to differ by treatment, as in Model (17), using

$$\begin{aligned} \text{poutcome}_{ijk} &\sim N(XB, \Omega) \\ \text{poutcome}_{ijk} &= 16.305(1.154)\text{constant} + -1.525(1.391)\text{study_id3}_k + -0.956(1.376)\text{study_id6}_k + 0.721(1.312)\text{study_id7}_k + \\ &\quad \beta_{4i}\text{treatment}_{jk} + e_{5ijk}\text{control}_{jk} \\ \beta_{4i} &= -2.465(0.897) + e_{4ijk} \end{aligned}$$

$$\begin{bmatrix} e_{4ijk} \\ e_{5ijk} \end{bmatrix} \sim N(0, \Omega_e) : \Omega_e = \begin{bmatrix} 82.111(7.759) & \\ 0.000(0.000) & 102.913(9.472) \end{bmatrix}$$

$-2*\text{loglikelihood(IGLS Deviance)} = 3381.428(460 \text{ of } 460 \text{ cases in use})$

where the constant is a fixed parameter only, while the control indicator variable is a level 1 term without a fixed parameter.

The fixed-effects meta-analysis corresponding to the two-level heteroscedastic model, given in Model (18), was fitted with

$$\begin{aligned} \text{poutcome}_{ijk} &\sim N(XB, \Omega) \\ \text{poutcome}_{ijk} &= 15.749(1.245)\text{constant} + -0.540(1.659)\text{study_id3}_k + 0.091(1.544)\text{study_id6}_k + 0.926(1.484)\text{study_id7}_k + \\ &\quad \beta_{4ij}\text{treatment}_{jk} + e_{5ijk}\text{control}_{jk} \\ \beta_{4ij} &= -2.458(1.116) + u_{4jk} + e_{4ijk} \end{aligned}$$

$$[u_{4jk}] \sim N(0, \Omega_u) : \Omega_u = [12.531(6.411)]$$

$$\begin{bmatrix} e_{4ijk} \\ e_{5ijk} \end{bmatrix} \sim N(0, \Omega_e) : \Omega_e = \begin{bmatrix} 73.198(7.451) & \\ 0.000(0.000) & 102.198(9.408) \end{bmatrix}$$

$-2*\text{loglikelihood(IGLS Deviance)} = 3376.944(460 \text{ of } 460 \text{ cases in use})$

while the random-effects meta-analysis, given in Model (19), was fitted using

$$\begin{aligned} \text{poutcome}_{ijk} &\sim N(XB, \Omega) \\ \text{poutcome}_{ijk} &= 15.408(1.361)\text{constant} + -0.061(1.820)\text{study_id3}_k + 0.972(1.738)\text{study_id6}_k + 0.943(1.669)\text{study_id7}_k + \\ &\quad \beta_{4ijk}\text{treatment}_{jk} + e_{5ijk}\text{control}_{jk} \\ \beta_{4ijk} &= -2.507(1.452) + v_{4k} + u_{4jk} + e_{4ijk} \end{aligned}$$

$$[v_{4k}] \sim N(0, \Omega_v) : \Omega_v = [3.560(4.758)]$$

$$[u_{4jk}] \sim N(0, \Omega_u) : \Omega_u = [11.203(6.540)]$$

$$\begin{bmatrix} e_{4ijk} \\ e_{5ijk} \end{bmatrix} \sim N(0, \Omega_e) : \Omega_e = \begin{bmatrix} 73.241(7.457) & \\ 0.000(0.000) & 101.865(9.377) \end{bmatrix}$$

$-2*\text{loglikelihood(IGLS Deviance)} = 3377.677(460 \text{ of } 460 \text{ cases in use})$

In order to fit the meta-regression models in Table 3, indicator variables `broad_treat`, `broad_cont`, `narrow_treat`, `narrow_cont` for the treatment-by-patient eligibility interaction and `man_treat`, `noman_treat` for the treatment-by-standardisation interaction were first added to the dataset. The fixed-effect meta-regression for the patient-level variance is given as:

$$poutcome_{ijk} \sim N(XB, \Omega)$$

$$poutcome_{ijk} = 15.726(1.164)constant + -0.557(1.540)study_id3_k + -0.499(1.513)study_id6_k + 0.903(1.387)study_id7_k + \beta_{4j}treatment_{jk} \\ + e_{5ijk}broad_treat_{jk} + e_{6ijk}broad_cont_{jk} + e_{7ijk}narrow_treat_{jk} + e_{8ijk}narrow_cont_{jk} \\ \beta_{4j} = -2.373(1.050) + u_{4jk}$$

$$\begin{bmatrix} u_{4jk} \end{bmatrix} \sim N(0, \Omega_u) : \Omega_u = \begin{bmatrix} 8.624(5.217) \end{bmatrix}$$

$$\begin{bmatrix} e_{5ijk} \\ e_{6ijk} \\ e_{7ijk} \\ e_{8ijk} \end{bmatrix} \sim N(0, \Omega_e) : \Omega_e = \begin{bmatrix} 80.712(9.307) & & & \\ 0.000(0.000) & 86.914(9.318) & & \\ 0.000(0.000) & 0.000(0.000) & 53.318(10.924) & \\ 0.000(0.000) & 0.000(0.000) & 0.000(0.000) & 142.062(25.518) \end{bmatrix}$$

-2*loglikelihood(IGLS Deviance) = 3368.216(460 of 460 cases in use)

While the fixed-effect meta-regression for the counsellor-level variance is given as:

$$poutcome_{ijk} \sim N(XB, \Omega)$$

$$poutcome_{ijk} = 15.842(1.268)constant + -0.578(1.375)study_id3_k + -0.151(1.452)study_id6_k + 0.861(1.591)study_id7_k + \beta_{4j}treatment_{jk} \\ + e_{5ijk}control_{jk} + u_{6jk}man_treat_{jk} \\ \beta_{4j} = -3.576(0.905) + u_{4jk} + e_{4ijk}$$

$$\begin{bmatrix} u_{4jk} \\ u_{6jk} \end{bmatrix} \sim N(0, \Omega_u) : \Omega_u = \begin{bmatrix} 28.188(14.074) \\ -15.138(7.026) & 0.000(0.000) \end{bmatrix}$$

$$\begin{bmatrix} e_{4ijk} \\ e_{5ijk} \end{bmatrix} \sim N(0, \Omega_e) : \Omega_e = \begin{bmatrix} 71.708(7.120) \\ 0.000(0.000) & 102.133(9.403) \end{bmatrix}$$

-2*loglikelihood(IGLS Deviance) = 3364.334(460 of 460 cases in use)

The parameterisation was altered to include a covariance term to avoid computational problems arising from a negative counsellor-level variance observed if counselling was standardised.