Multivariate Meta-Analysis for Longevity and Reproduction

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```r
# VCV matrix. Let's set up the multivariate meta-analysis model. We first need to create the VCV sampli

# V <- metafor::vcalc(vi=v, cluster = trial, subgroup = Experiment.code, type = outcome, data = data_lo

# First, lets capture the outcome covariance
  V_1 <- make_VCV_matrix(data = data_long_final, cluster = "trial",  V = "v", rho = 0.5)

# Using this matrix, we can now capture the shared control. here, we now just feed in the V matrix we j
  V <- metaAidR::make_VCV_matrix(data = data_long_final, matrix = V_1, cluster = "shared_control",  V =

# Export V matrix for checking
  write.csv(V, here("Output", "tables", "V.csv"))

# Check that this is set up correctly. Note that there are warnings about non-positive definite matrix.
  #V[1:15, 1:15]

  #corrplot(cov2cor(V)) # Takes a while so no need to run all the time

# Check of PD
  corpcor::is.positive.definite(V) # FALSE
```

```
## [1] FALSE
```

```r
# Can bend it to make it PD
  V <- Matrix::nearPD(V)$mat

# Check of PD
  corpcor::is.positive.definite(V) # TRUE
```

```
## [1] TRUE
```

```
##
## Multivariate Meta-Analysis Model (k = 1584; method: REML)
##
## Variance Components:
##
## outer factor: trial   (nlvls = 792)
## inner factor: outcome (nlvls = 2)
##
##            estim    sqrt  k.lvl  fixed           level
## tau^2.1   6.3326  2.5165    792     no      es_longevity
## tau^2.2   5.1975  2.2798    792     no   es_reproduction
##
##                 rho.es_l  rho.es_r    es_l  es_r
## es_longevity           1                 -   792
```

```
## es_reproduction      0.2515          1       no      -
##
## outer factor: Paper.code (nlvls = 200)
## inner factor: outcome    (nlvls = 2)
##
##                estim    sqrt  k.lvl  fixed          level
## gamma^2.1    0.4077  0.6386    792     no    es_longevity
## gamma^2.2    1.8133  1.3466    792     no  es_reproduction
##
##                 phi.es_l  phi.es_r   es_l  es_r
## es_longevity           1    0.5018      -   200
## es_reproduction   0.5018         1     no     -
##
## Test for Residual Heterogeneity:
## QE(df = 1582) = 1371482551.3700, p-val < .0001
##
## Test of Moderators (coefficients 1:2):
## F(df1 = 2, df2 = 398) = 43.9012, p-val < .0001
##
## Model Results:
##
##                       estimate      se     tval   df    pval    ci.lb
## outcomees_longevity    -0.0762  0.1059  -0.7196  398  0.4722  -0.2844
## outcomees_reproduction -1.2097  0.1330  -9.0918  398  <.0001  -1.4712
##                          ci.ub
## outcomees_longevity     0.1320
## outcomees_reproduction -0.9481  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Multivariate Meta-Analysis Model (k = 1584; method: REML)
##
## Variance Components:
##
## outer factor: trial   (nlvls = 792)
## inner factor: outcome (nlvls = 2)
##
##            estim    sqrt  k.lvl  fixed          level
## tau^2.1   4.1076  2.0267    792     no    es_longevity
## tau^2.2   5.0769  2.2532    792     no  es_reproduction
##
##               rho.es_l  rho.es_r   es_l  es_r
## es_longevity         1                -   792
## es_reproduction 0.1745         1     no     -
##
## outer factor: Paper.code (nlvls = 200)
## inner factor: outcome    (nlvls = 2)
##
##             estim    sqrt  k.lvl  fixed          level
## gamma^2.1  0.5118  0.7154    792     no    es_longevity
## gamma^2.2  1.7150  1.3096    792     no  es_reproduction
##
```

```
##                   phi.es_l  phi.es_r    es_l  es_r
## es_longevity             1    0.3702       -   200
## es_reproduction    0.3702         1      no     -
##
## Test for Residual Heterogeneity:
## QE(df = 1580) = 960835454.9878, p-val < .0001
##
## Test of Moderators (coefficients 2:4):
## F(df1 = 3, df2 = 396) = 132.5729, p-val < .0001
##
## Model Results:
##
##                                 estimate       se      tval     df    pval
## intrcpt                          -0.2224   0.0947   -2.3488    196  0.0198
## outcomees_reproduction           -1.0360   0.1407   -7.3613    396  <.0001
## c_treattemp                      -0.1815   0.0100  -18.2150    788  <.0001
## outcomees_reproduction:c_treattemp  0.1217  0.0137    8.8807   1580  <.0001
##                                   ci.lb    ci.ub
## intrcpt                         -0.4092  -0.0357     *
## outcomees_reproduction          -1.3127  -0.7593   ***
## c_treattemp                     -0.2011  -0.1619   ***
## outcomees_reproduction:c_treattemp  0.0949   0.1486  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Multivariate Meta-Analysis Model (k = 1584; method: REML)
##
## Variance Components:
##
## outer factor: trial    (nlvls = 792)
## inner factor: outcome (nlvls = 2)
##
##             estim    sqrt  k.lvl  fixed             level
## tau^2.1    4.1076  2.0267    792     no      es_longevity
## tau^2.2    5.0769  2.2532    792     no   es_reproduction
##
##                 rho.es_l  rho.es_r    es_l  es_r
## es_longevity           1                -   792
## es_reproduction   0.1745         1      no     -
##
## outer factor: Paper.code (nlvls = 200)
## inner factor: outcome    (nlvls = 2)
##
##               estim    sqrt  k.lvl  fixed             level
## gamma^2.1    0.5118  0.7154    792     no      es_longevity
## gamma^2.2    1.7150  1.3096    792     no   es_reproduction
##
##                   phi.es_l  phi.es_r    es_l  es_r
## es_longevity             1    0.3702       -   200
## es_reproduction    0.3702         1      no     -
##
## Test for Residual Heterogeneity:
```

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```
## QE(df = 1580) = 960835454.9878, p-val < .0001
##
## Test of Moderators (coefficients 1:4):
## F(df1 = 4, df2 = 396) = 105.4668, p-val < .0001
##
## Model Results:
##
##                                   estimate      se      tval    df    pval
## outcomees_longevity                -0.2224  0.0947   -2.3488   396  0.0193
## outcomees_reproduction             -1.2585  0.1308   -9.6250   396  <.0001
## outcomees_longevity:c_treattemp    -0.1815  0.0100  -18.2150  1580  <.0001
## outcomees_reproduction:c_treattemp -0.0598  0.0117   -5.1013  1580  <.0001
##                                     ci.lb    ci.ub
## outcomees_longevity                -0.4086  -0.0363    *
## outcomees_reproduction             -1.5155  -1.0014   ***
## outcomees_longevity:c_treattemp    -0.2010  -0.1620   ***
## outcomees_reproduction:c_treattemp -0.0827  -0.0368   ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
# We'll now run the multivariate model with non-linear terms as was done in the univariate cases.
rerun2=FALSE
if(rerun2){
  mv_mlma_4 <- rma.mv(es ~ -1 + outcome + outcome:poly(c_treattemp, degree=3, raw=TRUE), V = V,
             random = list(~outcome - 1 | trial,       # This would be equivalent to an obs level ra
                           ~outcome - 1 | Paper.code),  # This should estimate a study level random e
             struc = "UN", data = data_long_final, test = "t", dfs = "contain")
  saveRDS(mv_mlma_4, here("output", "models", "mv_mlma_4.rds"))
} else {
  mv_mlma_4 <- readRDS(here("output", "models", "mv_mlma_4.rds"))
}
  mv_mlma_4
```

```
##
## Multivariate Meta-Analysis Model (k = 1584; method: REML)
##
## Variance Components:
##
## outer factor: trial    (nlvls = 792)
## inner factor: outcome (nlvls = 2)
##
##            estim    sqrt  k.lvl  fixed             level
## tau^2.1   3.8943  1.9734    792     no       es_longevity
## tau^2.2   4.0886  2.0220    792     no    es_reproduction
##
##                 rho.es_l  rho.es_r   es_l   es_r
## es_longevity           1         -    792
## es_reproduction   0.1513         1     no      -
##
## outer factor: Paper.code (nlvls = 200)
## inner factor: outcome    (nlvls = 2)
##
##              estim    sqrt  k.lvl  fixed             level
## gamma^2.1   0.4708  0.6862    792     no       es_longevity
```

```
## gamma^2.2    2.4585  1.5679    792    no  es_reproduction
##
##                 phi.es_l  phi.es_r    es_l  es_r
## es_longevity           1    0.4889       -   200
## es_reproduction   0.4889         1      no     -
##
## Test for Residual Heterogeneity:
## QE(df = 1576) = 933779437.2520, p-val < .0001
##
## Test of Moderators (coefficients 1:8):
## F(df1 = 8, df2 = 392) = 71.9910, p-val < .0001
##
## Model Results:
##
##                                                             estimate
## outcomees_longevity                                          -0.0903
## outcomees_reproduction                                       -0.4837
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)1    -0.2581
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)1    -0.0660
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)2    -0.0022
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)2   -0.0123
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)3     0.0005
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)3   -0.0001
##                                                                  se
## outcomees_longevity                                          0.1113
## outcomees_reproduction                                       0.1579
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)1    0.0150
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)1 0.0162
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)2    0.0010
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)2 0.0012
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)3    0.0001
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)3 0.0001
##                                                                tval
## outcomees_longevity                                          -0.8111
## outcomees_reproduction                                       -3.0626
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)1   -17.2650
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)1   -4.0714
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)2    -2.1196
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)2 -10.2060
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)3     6.4821
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)3   -0.8122
##                                                                df    pval
## outcomees_longevity                                          392  0.4178
## outcomees_reproduction                                       392  0.0023
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)1   1576  <.0001
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)1  1576  <.0001
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)2   1576  0.0342
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)2  1576  <.0001
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)3   1576  <.0001
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)3  1576  0.4168
##                                                                ci.lb
## outcomees_longevity                                          -0.3092
## outcomees_reproduction                                       -0.7943
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)1    -0.2875
```

```
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)1  -0.0978
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)2     -0.0042
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)2  -0.0146
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)3      0.0003
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)3  -0.0002
##                                                                        ci.ub
## outcomees_longevity                                                   0.1286
## outcomees_reproduction                                               -0.1732   **
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)1       -0.2288  ***
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)1   -0.0342  ***
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)2       -0.0002    *
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)2   -0.0099  ***
## outcomees_longevity:poly(c_treattemp, degree = 3, raw = TRUE)3        0.0006  ***
## outcomees_reproduction:poly(c_treattemp, degree = 3, raw = TRUE)3    0.0001
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
# We can get confidence intervals by profiling the liklihood
  if(rerun2){
  cis <- confint(mv_mlma_4, rho = 1)
  write.csv(cis, here("output", "tables", "mv_mlma_4_cis.csv"))
  } else {
    cis <- read.csv(here("output", "tables", "mv_mlma_4_cis.csv"))
  }
 cis
```

```
## [1] X  X1 X2 X3
## <0 rows> (or 0-length row.names)
```

```r
# Lets explore the among study correlation.
data %>% group_by(Experiment.code) %>% summarise(es_repro = mean(es_reproduction), es_long = mean(es_
```

```
## Warning: Returning more (or less) than 1 row per `summarise()` group was deprecated in
## dplyr 1.1.0.
## i Please use `reframe()` instead.
## i When switching from `summarise()` to `reframe()`, remember that `reframe()`
##   always returns an ungrouped data frame and adjust accordingly.
## Call `lifecycle::last_lifecycle_warnings()` to see where this warning was
## generated.
```

```
## `summarise()` has grouped output by 'Experiment.code'. You can override using
## the `.groups` argument.
```