

# Meta-Analysis for Longevity Summary Excluding HUM251

Fay Frost

## 1. Summary

This document reports the process taken in the model fitting stage of the meta-analysis in thermal longevity.

## 2. Setup

We first read in our data and select all of the effect sizes related to longevity. We do this using the following code.

```
### Read in effect size data
effectdata <- read.csv("Survival project all pairwise.es.csv")
longdata_warm <- subset(effectdata, Trait.category == "Longevity" &
  warm.cool == "Warm")
longdata_cool <- subset(effectdata, Trait.category == "Longevity" &
  warm.cool == "Cool")

alllong <- rbind(longdata_warm, longdata_cool)

### select data for analysis
rdata <- alllong

rdata <- subset(rdata, Paper.code != "HUM251")
```

Next we create new columns in our dataframe which will serve as random factors in our multi-level meta analysis models. The following initialises four new columns, namely “obs”, “study\_code”, “Species.phylo” and “species”. Lastly, we create a column name “precision” which is equal to the inverse standard error.

```
### Create random factors into data frame
rdata$obs <- factor(c(1:nrow(rdata))) # Unique observation code
rdata$study_code <- factor(rdata$Paper.code) # Model requires column names study_code
rdata$Species.phylo <- factor(rdata$Species.latin) # Species names for phylo matrix
rdata$species <- factor(rdata$Species.latin) # Another species column for random factor

precision <- sqrt(1/rdata$v) # inverse standard error
rdata[, "precision"] <- precision
```

The number of species and total number of studies present in the data are as follows.

```
nlevels(rdata$species) # Check number of species

## [1] 290

nlevels(rdata$study_code) # Check number of studies

## [1] 316
```

The final stage in the setup is to import a phylogenetic tree of the data. Below is the code used to produce the tree and a plot of the tree itself.

```
## import tree from map
tree1 <- read.nexus("all_longevity_excHUM251_tree.nex")
tree_grafen = compute.brlen(tree1, method = "Grafen", power = 1)
phylo_matrix <- vcv(tree_grafen, cor = TRUE, model = "Brownian") # Make phylogenetic matrix

## character(0)
```



### 3. Random effects models

In this section we determine which random effects to include in our model. For each model I have provided the code used to specify the structure of the model and a summary of the results. We begin with a model that includes all of the random factors we created earlier.

```
# Adding four random factors
meta2 <- rma.mv(es, v, random = list(~1 | Species.phylo, ~1 |
  species, ~1 | study_code, ~1 | obs), R = list(Species.phylo = phylo_matrix),
  data = rdata, method = "REML")
```

```
summary(meta2)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3571.8849    7143.7698    7153.7698    7179.9227    7153.8135
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor      R
## sigma^2.1  0.0000  0.0001   290     no Species.phylo  yes
## sigma^2.2  0.0000  0.0003   290     no      species    no
## sigma^2.3  0.9550  0.9772   316     no  study_code    no
## sigma^2.4  7.6569  2.7671  1382     no        obs     no
##
## Test for Heterogeneity:
## Q(df = 1381) = 51324.4159, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -0.1790  0.0979  -1.8293  0.0674  -0.3708  0.0128
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
i2_ml(meta2, method = c("ratio")) # Heterogeneity at each random factor level
```

```
##      I2_Total I2_Species.phylo      I2_species      I2_study_code      I2_obs
##      9.908043e+01      4.914096e-08      1.311826e-06      1.098728e+01      8.809316e+01
```

#### Accounting for non-independence of data points from the same experiment

The data has a nested structure. Each study (study\_code) may have a number of experiments (effect.size.code) which share a common control temperature. Each effect size has its own unique code, obs. Effect sizes from the same experiment which share a control temperature are thought to be non-independent. The following code create a covariance matrix “VCV\_shared” which assumes a correlation of 0.5 between effect sizes from the same experiment. We include this structure in our proceeding models.

```
rdata$shared_control <- factor(rdata$Effect.size.code)
vcv_shared <- impute_covariance_matrix(vi = rdata$v, cluster = rdata$shared_control,
  r = 0.5)
```

```
# Add new variance matrix into the mixed-effects
# meta-analysis model
```

```
meta3 <- rma.mv(es, vcv_shared, random = list(~1 | Species.phylo,
~1 | species, ~1 | study_code, ~1 | shared_control, ~1 |
obs), R = list(Species.phylo = phylo_matrix), data = rdata,
method = "REML")
```

```
summary(meta3)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3560.9037    7121.8074    7133.8074    7165.1908    7133.8686
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor      R
## sigma^2.1  0.0000  0.0005   290    no  Species.phylo  yes
## sigma^2.2  0.0000  0.0005   290    no      species    no
## sigma^2.3  0.6814  0.8255   316    no   study_code    no
## sigma^2.4  0.0000  0.0001   438    no shared_control  no
## sigma^2.5  7.9209  2.8144  1382    no      obs        no
##
## Test for Heterogeneity:
## Q(df = 1381) = 69576.2623, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -0.1908  0.0946  -2.0175  0.0436  -0.3762  -0.0054  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
i2_ml(meta3, method = c("ratio")) # Heterogeneity at each random factor level
```

```
##      I2_Total  I2_Species.phylo      I2_species  I2_study_code  I2_shared_control
##      9.907941e+01      3.442437e-06  3.218811e-06  7.848050e+00  4.708967e-08  9.123
```

## Model without phylogeny

The variance-covariance matrix for phylogenetic relatedness of included species has now been excluded as a random effect in the model (Chamberlain et al., 2012) as its inclusion did not improve model fit and the phylogenetic signal was very weak.

```
## without phylogeny but with shared control
meta5 <- rma.mv(es, VCV_shared, random = list(~1 | species, ~1 |
  study_code, ~1 | shared_control, ~1 | obs), data = rdata,
  method = "REML")
```

```
summary(meta5)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3560.9037    7121.8074    7131.8074    7157.9603    7131.8511
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.0000  0.0003   290     no      species
## sigma^2.2  0.6814  0.8255   316     no      study_code
## sigma^2.3  0.0000  0.0000   438     no      shared_control
## sigma^2.4  7.9209  2.8144  1382     no      obs
##
## Test for Heterogeneity:
## Q(df = 1381) = 69576.2623, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -0.1908  0.0946  -2.0175   0.0436  -0.3762  -0.0054  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
i2_ml(meta5, method = c("ratio")) # Heterogeneity at each random factor level
```

```
##      I2_Total      I2_species      I2_study_code I2_shared_control      I2_obs
##      9.907941e+01      7.628247e-07      7.848052e+00      1.543144e-08      9.123136e+01
```

## Model without phylogeny or species

```
## without phylogeny or species
meta4 <- rma.mv(es, VCV_shared, random = list(~1 | study_code,
~1 | shared_control, ~1 | obs), data = rdata, method = "REML")

summary(meta4)

##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3560.9037    7121.8074    7129.8074    7150.7297    7129.8365
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.6814  0.8255   316     no      study_code
## sigma^2.2  0.0000  0.0001   438     no    shared_control
## sigma^2.3  7.9209  2.8144  1382     no          obs
##
## Test for Heterogeneity:
## Q(df = 1381) = 69576.2623, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -0.1908  0.0946  -2.0175  0.0436  -0.3762  -0.0054  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

i2_ml(meta4, method = c("ratio")) # Heterogeneity at each random factor level

##      I2_Total      I2_study_code I2_shared_control      I2_obs
##      9.907941e+01      7.848054e+00      2.153089e-07      9.123136e+01
```

## Model without phylogeny, species or study\_code

```
## without phylogeny, species or study_code
meta7 <- rma.mv(es, VCV_shared, random = list(~1 | shared_control,
~1 | obs), data = rdata, method = "REML")
```

```
summary(meta7)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3578.7983    7157.5966    7163.5966    7179.2883    7163.6140
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.2783  0.5276   438     no  shared_control
## sigma^2.2  8.4433  2.9057  1382     no           obs
##
## Test for Heterogeneity:
## Q(df = 1381) = 69576.2623, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -0.2099  0.0852  -2.4643  0.0137  -0.3769  -0.0430  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
i2_ml(meta7, method = c("ratio")) # Heterogeneity at each random factor level
```

```
##      I2_Total  I2_shared_control      I2_obs
##      99.091897      3.162119      95.929777
```

## Model without phylogeny, species or shared\_control

```
## without phylogeny, species or shared_control
meta8 <- rma.mv(es, VCV_shared, random = list(~1 | study_code,
~1 | obs), data = rdata, method = "REML")
```

```
summary(meta8)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3560.9037    7121.8074    7127.8074    7143.4991    7127.8249
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.6814  0.8255   316      no  study_code
## sigma^2.2  7.9209  2.8144  1382      no      obs
##
## Test for Heterogeneity:
## Q(df = 1381) = 69576.2623, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -0.1908  0.0946  -2.0175  0.0436  -0.3762  -0.0054  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
i2_ml(meta8, method = c("ratio")) # Heterogeneity at each random factor level
```

```
##      I2_Total I2_study_code      I2_obs
##      99.079415      7.848054    91.231361
```

We can see from the above that the best fitting model according to AIC is “meta8” which includes only the study code and the unique effect size code, obs. However, since there is not a huge difference ( $\Delta \text{AIC} = 2$ ) between the AIC of this model and “meta4” which also includes shared\_control, we choose to proceed with meta4. The thought being that



## 4. Meta-regressions

Starting with the best fitting random-effect model from Section 3, “meta4” we now include single factors as a fixed effect. We initially explore the fixed factors

- **reftemp**: The experiment’s control (reference) temperature.
- **treattemp**: The treatment temperature, which we expect to have a non-linear relationship to longevity.
- **warm.cool**: A categorical variable indicating whether treatment is warmer or cooler than the reference temperature
- **diff**: The difference between the reference and treatment temperature.

### Reference temperature

```
meta_trait_ref <- rma.mv(es, VCV_shared, mod = ~reftemp, random = list(~1 |
  study_code, ~1 | shared_control, ~1 | obs), data = rdata,
  method = "REML")
```

```
summary(meta_trait_ref)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3557.9855    7115.9711    7125.9711    7152.1203    7126.0147
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.6735  0.8207   316     no    study_code
## sigma^2.2  0.0000  0.0001   438     no  shared_control
## sigma^2.3  7.9237  2.8149  1382     no           obs
##
## Test for Residual Heterogeneity:
## QE(df = 1380) = 69511.6772, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 1.5365, p-val = 0.2151
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt    -1.3027  0.9019  -1.4443  0.1486   -3.0705   0.4651
## reftemp     0.0447  0.0361   1.2396  0.2151   -0.0260   0.1154
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

## Treatment temperature

```
meta_trait_treattemp <- rma.mv(es, VCV_shared, mod = ~treattemp,  
  random = list(~1 | study_code, ~1 | shared_control, ~1 |  
    obs), data = rdata, method = "REML")
```

```
summary(meta_trait_treattemp)
```

```
##  
## Multivariate Meta-Analysis Model (k = 1382; method: REML)  
##  
##      logLik      Deviance      AIC      BIC      AICc  
## -3358.7934    6717.5868    6727.5868    6753.7360    6727.6304  
##  
## Variance Components:  
##  
##      estim      sqrt  nlvls  fixed      factor  
## sigma^2.1  1.1310  1.0635   316     no      study_code  
## sigma^2.2  0.0000  0.0002   438     no  shared_control  
## sigma^2.3  5.3085  2.3040  1382     no           obs  
##  
## Test for Residual Heterogeneity:  
## QE(df = 1380) = 48881.9211, p-val < .0001  
##  
## Test of Moderators (coefficient 2):  
## QM(df = 1) = 490.1334, p-val < .0001  
##  
## Model Results:  
##  
##      estimate      se      zval      pval      ci.lb      ci.ub  
## intrcpt      4.4550  0.2295   19.4086 <.0001    4.0051    4.9049 ***  
## treattemp    -0.1907  0.0086  -22.1390 <.0001   -0.2076   -0.1739 ***  
##  
## ---  
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

## Warm vs Cool

```
meta_trait_warm <- rma.mv(es, VCV_shared, mod = ~warm.cool, random = list(~1 |  
  study_code, ~1 | shared_control, ~1 | obs), data = rdata,  
  method = "REML")
```

```
summary(meta_trait_warm)
```

```
##  
## Multivariate Meta-Analysis Model (k = 1382; method: REML)  
##  
##      logLik      Deviance      AIC      BIC      AICc  
## -3327.9584    6655.9167    6665.9167    6692.0659    6665.9604  
##  
## Variance Components:  
##  
##      estim      sqrt  nlvls  fixed      factor  
## sigma^2.1  0.6253  0.7908   316     no      study_code  
## sigma^2.2  0.0000  0.0001   438     no  shared_control  
## sigma^2.3  5.2711  2.2959  1382     no              obs  
##  
## Test for Residual Heterogeneity:  
## QE(df = 1380) = 46543.7238, p-val < .0001  
##  
## Test of Moderators (coefficient 2):  
## QM(df = 1) = 557.6079, p-val < .0001  
##  
## Model Results:  
##  
##      estimate      se      zval      pval      ci.lb      ci.ub  
## intrcpt          1.3460  0.1047   12.8579 <.0001    1.1408    1.5511 ***  
## warm.coolWarm   -3.0955  0.1311  -23.6137 <.0001   -3.3524   -2.8386 ***  
##  
## ---  
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

We model warm versus cool without and intercept so we can visualise the estimates easier.

```
meta_trait_warm_nointer <- rma.mv(es, VCV_shared, mod = ~warm.cool -
  1, random = list(~1 | study_code, ~1 | shared_control, ~1 |
    obs), data = rdata, method = "REML")

summary(meta_trait_warm_nointer)

##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3327.9584   6655.9167   6665.9167   6692.0659   6665.9604
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.6253  0.7908   316    no      study_code
## sigma^2.2  0.0000  0.0001   438    no  shared_control
## sigma^2.3  5.2711  2.2959  1382    no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 1380) = 46543.7238, p-val < .0001
##
## Test of Moderators (coefficients 1:2):
## QM(df = 2) = 563.3163, p-val < .0001
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## warm.coolCool    1.3460  0.1047   12.8579  <.0001    1.1408    1.5511 ***
## warm.coolWarm   -1.7495  0.1050  -16.6603  <.0001   -1.9554   -1.5437 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

## Difference

```
meta_trait_diff <- rma.mv(es, VCV_shared, mod = ~diff, random = list(~1 |  
  study_code, ~1 | shared_control, ~1 | obs), data = rdata,  
  method = "REML")
```

```
summary(meta_trait_diff)
```

```
##  
## Multivariate Meta-Analysis Model (k = 1382; method: REML)  
##  
##      logLik      Deviance      AIC      BIC      AICc  
## -3345.2685    6690.5369    6700.5369    6726.6861    6700.5806  
##  
## Variance Components:  
##  
##      estim      sqrt  nlvls  fixed      factor  
## sigma^2.1  0.9862  0.9931   316     no      study_code  
## sigma^2.2  0.0000  0.0002   438     no  shared_control  
## sigma^2.3  5.2472  2.2907  1382     no              obs  
##  
## Test for Residual Heterogeneity:  
## QE(df = 1380) = 46607.4493, p-val < .0001  
##  
## Test of Moderators (coefficient 2):  
## QM(df = 1) = 521.4648, p-val < .0001  
##  
## Model Results:  
##  
##      estimate      se      zval      pval      ci.lb      ci.ub  
## intrcpt    -0.2828  0.0894   -3.1642  0.0016   -0.4579   -0.1076   **  
## diff       -0.1969  0.0086  -22.8356 <.0001   -0.2138   -0.1800   ***  
##  
## ---  
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

## Treatment temperature as a cubic effect

We expect that treatment temperature will have a non-linear effect on longevity. We expect that the relationship will be cubic. More specifically, we expect that longevity will increase at cooler temperature and decrease at more extreme higher temperature. We also assume that this optimum temperature will be close to the control temperature. That said, we investigate **treattemp** as a cubic fixed effect.

```
meta_trait_treat3 <- rma.mv(es, VCV_shared, mod = ~poly(treattemp,
  degree = 3, raw = TRUE), random = list(~1 | study_code, ~1 |
  shared_control, ~1 | obs), data = rdata, method = "REML")
```

```
summary(meta_trait_treat3)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3290.8494    6581.6988    6595.6988    6632.2975    6595.7805
##
## Variance Components:
##
##      estim      sqrt      nlvls      fixed      factor
## sigma^2.1  0.6616  0.8134    316      no      study_code
## sigma^2.2  0.0000  0.0001    438      no      shared_control
## sigma^2.3  4.9896  2.2337   1382      no      obs
##
## Test for Residual Heterogeneity:
## QE(df = 1378) = 45378.7194, p-val < .0001
##
## Test of Moderators (coefficients 2:4):
## QM(df = 3) = 651.9762, p-val < .0001
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt          -4.8530  0.8125   -5.9729 <.0001   -6.4454   -3.2605 ***
## poly(treattemp, degree = 3, raw = TRUE)1    1.0759  0.1072   10.0360 <.0001    0.8658    1.2861 ***
## poly(treattemp, degree = 3, raw = TRUE)2   -0.0515  0.0045  -11.4015 <.0001   -0.0604   -0.0427 ***
## poly(treattemp, degree = 3, raw = TRUE)3    0.0006  0.0001   10.6342 <.0001    0.0005    0.0008 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

For completeness we also investigate treatment temperature as a quadratic effect.

```
meta_trait_treat2 <- rma.mv(es, VCV_shared, mod = ~poly(treattemp,
  degree = 2, raw = TRUE), random = list(~1 | study_code, ~1 |
  shared_control, ~1 | obs), data = rdata, method = "REML")
```

```
summary(meta_trait_treat2)
```

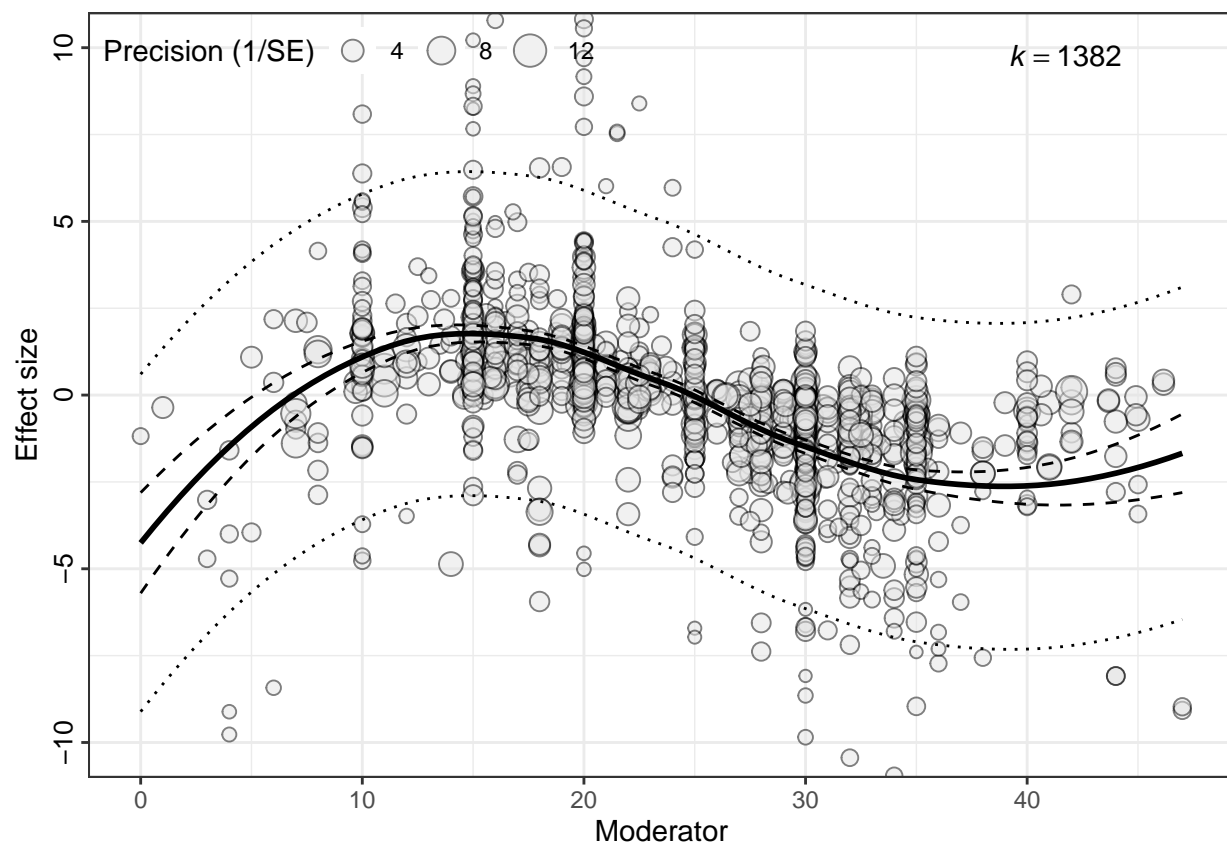
```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3344.0319    6688.0637    6700.0637    6731.4384    6700.1249
##
```

```

## Variance Components:
##
##      estim    sqrt  nlvls  fixed      factor
## sigma^2.1  1.1445  1.0698   316    no      study_code
## sigma^2.2  0.0000  0.0001   438    no  shared_control
## sigma^2.3  5.1947  2.2792  1382    no           obs
##
## Test for Residual Heterogeneity:
## QE(df = 1379) = 48695.5096, p-val < .0001
##
## Test of Moderators (coefficients 2:3):
## QM(df = 2) = 526.1208, p-val < .0001
##
## Model Results:
##
##              estimate      se    zval    pval    ci.lb    ci.ub
## intrcpt              2.0945  0.5185   4.0392 <.0001    1.0782    3.1108 ***
## poly(treattemp, degree = 2, raw = TRUE)1    0.0287  0.0441   0.6503  0.5155   -0.0577    0.1150
## poly(treattemp, degree = 2, raw = TRUE)2   -0.0045  0.0009  -5.0830 <.0001   -0.0063   -0.0028 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

```

Below is a bubble plot of the fitted cubic model.





## Modelling response with binned treatment temperatures

The last model we will try is one with categorised or ‘binned’ treatment temperatures. We categories our effect sizes into one seven bins depending on the treatment temperature. The bins and the number of effect sizes in each bin are given below

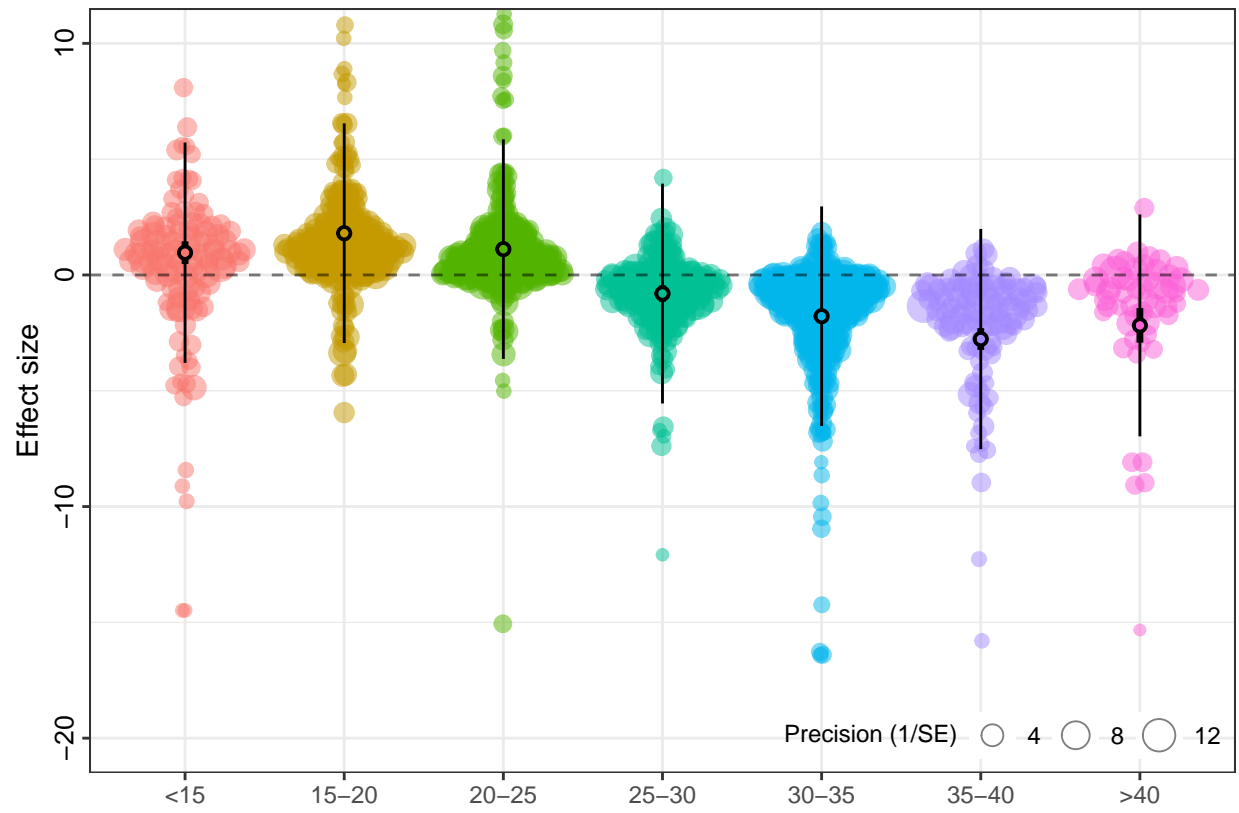
```
table(rdata$bin.temp)
```

```
##
##    <15    >40 15-20 20-25 25-30 30-35 35-40
##    110     55  249   316   189   354   109
```

```
meta_trait_bintemp <- rma.mv(es, VCV_shared, mod = ~bin.temp -
  1, random = list(~1 | study_code, ~1 | shared_control, ~1 |
  obs), data = rdata, method = "REML")
```

```
summary(meta_trait_bintemp)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3301.9785    6603.9571    6623.9571    6676.2192    6624.1184
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.7390  0.8597   316     no      study_code
## sigma^2.2  0.0000  0.0001   438     no  shared_control
## sigma^2.3  5.0896  2.2560  1382     no      obs
##
## Test for Residual Heterogeneity:
## QE(df = 1375) = 46258.1063, p-val < .0001
##
## Test of Moderators (coefficients 1:7):
## QM(df = 7) = 611.9859, p-val < .0001
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## bin.temp<15      0.9617  0.2502    3.8429  0.0001    0.4712    1.4521 ***
## bin.temp>40     -2.1784  0.3797   -5.7369 <.0001   -2.9226   -1.4342 ***
## bin.temp15-20     1.8017  0.1599   11.2702 <.0001    1.4883    2.1150 ***
## bin.temp20-25     1.1145  0.1434    7.7700 <.0001    0.8334    1.3957 ***
## bin.temp25-30    -0.8030  0.1822   -4.4066 <.0001   -1.1602   -0.4459 ***
## bin.temp30-35    -1.7813  0.1366  -13.0428 <.0001   -2.0490   -1.5136 ***
## bin.temp35-40    -2.7667  0.2393  -11.5591 <.0001   -3.2358   -2.2976 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```



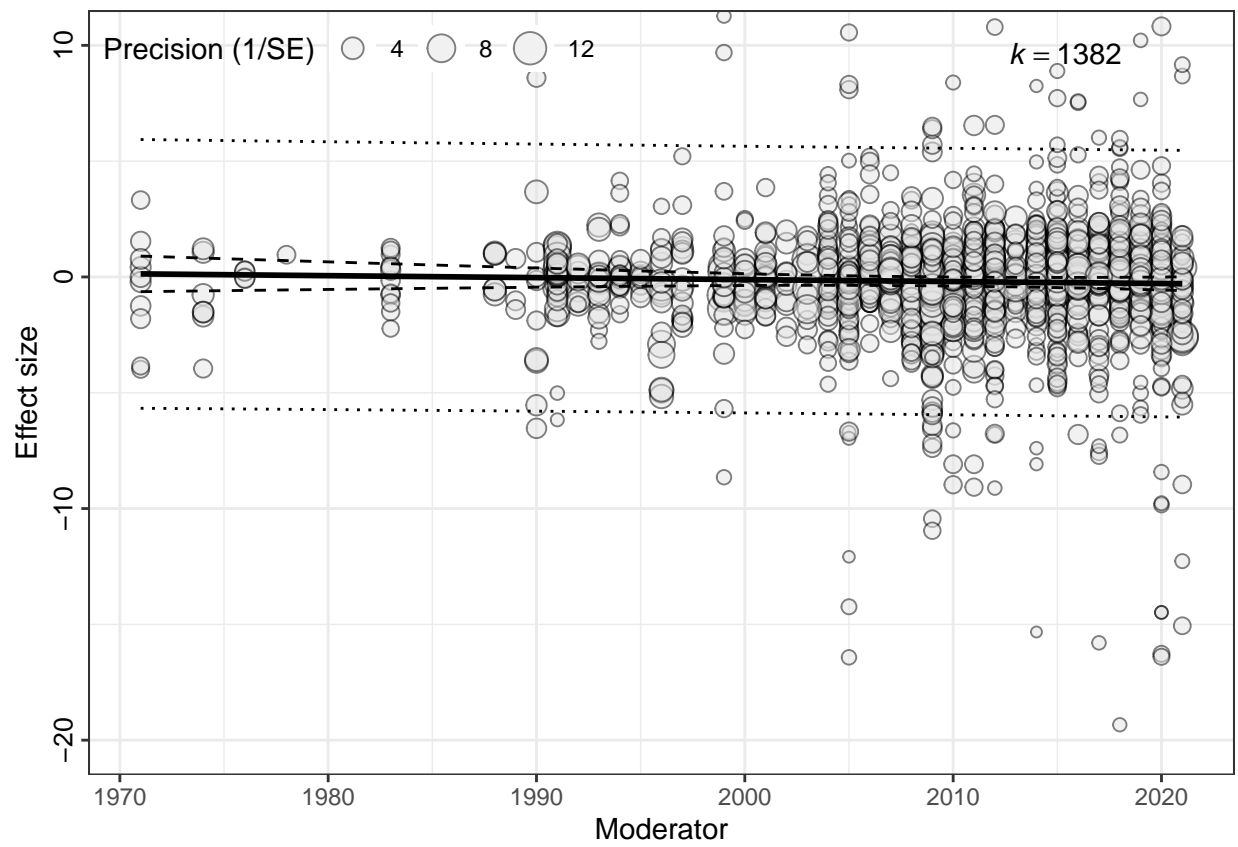
## Publication Bias.

We fit meta-regression model with year as a moderator to see whether there is an publication bias. In other words, is effect size strongly correlated with publication year. We found now evidence to suggest that year has an effect on the report effect sizes. A summary of the model is given below.

```
meta_year <- rma.mv(es, VCV_shared, mod = ~Publication.year,
  random = list(~1 | study_code, ~1 | shared_control, ~1 |
    obs), data = rdata, method = "REML")
```

```
summary(meta_year)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3558.3572    7116.7145    7126.7145    7152.8637    7126.7581
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.6925  0.8321   316    no      study_code
## sigma^2.2  0.0000  0.0001   438    no  shared_control
## sigma^2.3  7.9179  2.8139  1382    no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 1380) = 69484.5678, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 0.7240, p-val = 0.3948
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt      16.8319  20.0060   0.8413  0.4002  -22.3792  56.0430
## Publication.year -0.0085   0.0100  -0.8509  0.3948   -0.0280   0.0110
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```



## Sensitivity Analysis

Here, we perform a sensitivity analysis by removing the smallest and largest 2.5% of effect sizes.

The 2.5th and 97.5th percentiles are given below.

```
print(minq)
```

```
##      2.5%  
## -6.893544
```

```
print(maxq)
```

```
##      97.5%  
##  6.429868
```

The sumamry of the effect sizes is now

```
summary(sdata$es)
```

```
##      Min.  1st Qu.  Median    Mean 3rd Qu.    Max.  
## -6.82667 -1.23065 -0.07193 -0.18820  0.98166  6.37946
```

We run the cubic treatment temperature and the binned temperature models again with our new subsetted data i.e. only with data that is between the 2.5Th and 97.5Th percentile.

### Treatment temperature as a cubic effect (sesnsitivity analysis)

We re-create the variance-covariance matrix with our new subsetted data, which we name sdata. Then we run the meta analysis model again with treatment temperature as quadratic fixed effect.

```
# recreate vcv_shared matrix
```

```
VCV_shared_sa <- impute_covariance_matrix(vi = sdata$v, cluster = sdata$shared_control,  
  r = 0.5)
```

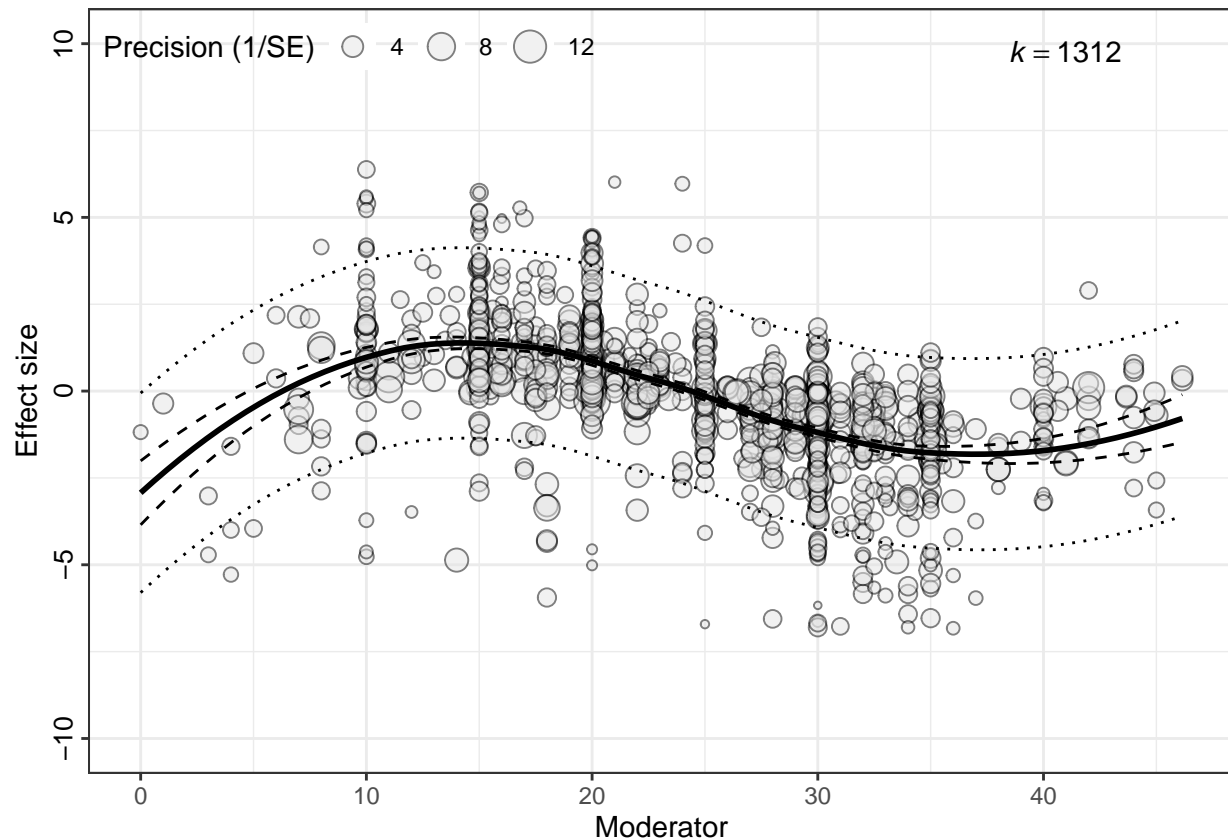
```
meta_sa_treat3 <- rma.mv(es, VCV_shared_sa, mod = ~poly(treattemp,  
  degree = 3, raw = TRUE), random = list(~1 | study_code, ~1 |  
  shared_control, ~1 | obs), data = sdata, method = "REML")
```

```
summary(meta_sa_treat3)
```

```
##  
## Multivariate Meta-Analysis Model (k = 1312; method: REML)  
##  
##      logLik      Deviance      AIC      BIC      AICc  
## -2304.7900  4609.5799  4623.5799  4659.8137  4623.6661  
##  
## Variance Components:  
##  
##      estim      sqrt  nlvls  fixed      factor  
## sigma^2.1  0.5097  0.7139   313    no      study_code  
## sigma^2.2  0.0170  0.1302   433    no  shared_control  
## sigma^2.3  1.4234  1.1931  1312    no          obs  
##  
## Test for Residual Heterogeneity:  
## QE(df = 1308) = 28247.0314, p-val < .0001  
##  
## Test of Moderators (coefficients 2:4):  
## QM(df = 3) = 1110.1810, p-val < .0001
```

```
##
## Model Results:
##
##               estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt          -3.3901  0.5147   -6.5863 <.0001   -4.3990   -2.3813 ***
## poly(treattemp, degree = 3, raw = TRUE)1    0.8103  0.0679   11.9354 <.0001    0.6773    0.9434 ***
## poly(treattemp, degree = 3, raw = TRUE)2   -0.0404  0.0029  -14.0167 <.0001   -0.0460   -0.0347 ***
## poly(treattemp, degree = 3, raw = TRUE)3    0.0005  0.0000   13.4033 <.0001    0.0004    0.0006 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Below is a bubble plot of the fitted cubic model to the subsetted data.



## Modelling response with binned treatment temperatures

Lastly, we rerun the model where our effect sizes are categorised into one seven bins depending on the treatment temperature. The bins and the number of effect sizes in each bin of the new subsetted data are given below

```
table(sdata$bin.temp)
```

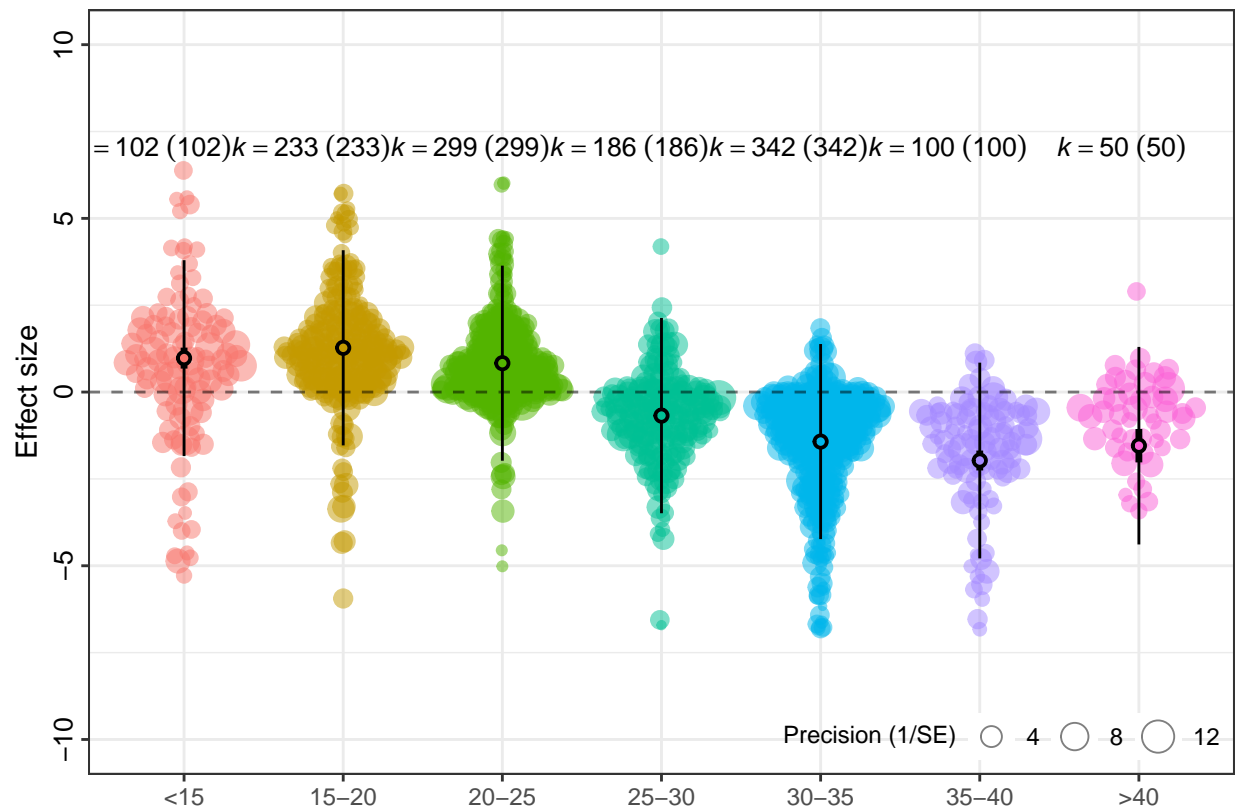
```
##
##  <15  >40 15-20 20-25 25-30 30-35 35-40
##  102   50  233  299  186  342  100
```

```
meta_sa_bintemp <- rma.mv(es, VCV_shared_sa, mod = ~bin.temp -
  1, random = list(~1 | study_code, ~1 | shared_control, ~1 |
  obs), data = sdata, method = "REML")
```

```
summary(meta_sa_bintemp)
```

```
##
## Multivariate Meta-Analysis Model (k = 1312; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -2327.1953  4654.3905  4674.3905  4726.1301  4674.5605
##
## Variance Components:
##
```

```
##          estim      sqrt  nlvls  fixed      factor
## sigma^2.1 0.5447  0.7380   313    no      study_code
## sigma^2.2 0.0000  0.0003   433    no  shared_control
## sigma^2.3 1.4996  1.2246  1312    no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 1305) = 29287.2564, p-val < .0001
##
## Test of Moderators (coefficients 1:7):
## QM(df = 7) = 1018.0860, p-val < .0001
##
## Model Results:
##
##          estimate      se      zval      pval      ci.lb      ci.ub
## bin.temp<15      0.9777  0.1539   6.3516 <.0001   0.6760   1.2794 ***
## bin.temp>40     -1.5433  0.2451  -6.2978 <.0001  -2.0237  -1.0630 ***
## bin.temp15-20     1.2741  0.0991  12.8584 <.0001   1.0799   1.4683 ***
## bin.temp20-25     0.8315  0.0894   9.2959 <.0001   0.6562   1.0068 ***
## bin.temp25-30    -0.6773  0.1094  -6.1912 <.0001  -0.8917  -0.4629 ***
## bin.temp30-35    -1.4249  0.0851 -16.7427 <.0001  -1.5917  -1.2581 ***
## bin.temp35-40    -1.9700  0.1462 -13.4740 <.0001  -2.2566  -1.6835 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```





## Other fixed effects

```
meta_bintemp_habitat <- rma.mv(es, VCV_shared, mod = ~bin.temp *
  Habitat, random = list(~1 | study_code, ~1 | shared_control,
    ~1 | obs), data = rdata, method = "REML")
```

```
summary(meta_bintemp_habitat)
```

```
##
## Multivariate Meta-Analysis Model (k = 1382; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3267.9085    6535.8170    6577.8170    6687.3987    6578.5055
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.5986  0.7737   316    no      study_code
## sigma^2.2  0.0000  0.0001   438    no  shared_control
## sigma^2.3  5.0815  2.2542  1382    no      obs
##
## Test for Residual Heterogeneity:
## QE(df = 1364) = 43855.7531, p-val < .0001
##
## Test of Moderators (coefficients 2:18):
## QM(df = 17) = 638.5658, p-val < .0001
##
## Model Results:
##
##              estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt          -0.3771  1.4055   -0.2683  0.7885   -3.1318   2.3775
## bin.temp>40        -3.1842  0.4477   -7.1124 <.0001   -4.0617  -2.3068 ***
## bin.temp15-20        2.2450  1.5222    1.4749  0.1402   -0.7383   5.2284
## bin.temp20-25        1.9369  1.6146    1.1996  0.2303   -1.2277   5.1015
## bin.temp25-30       -1.6073  1.4998   -1.0717  0.2839   -4.5468   1.3322
## bin.temp30-35       -0.3674  1.7226   -0.2133  0.8311   -3.7436   3.0088
## bin.temp35-40       -3.8153  0.3425  -11.1404 <.0001   -4.4866  -3.1441 ***
## HabitatBoth        -4.2720  2.2020   -1.9400  0.0524   -8.5880   0.0439 .
## HabitatTerrestrial    1.4759  1.4281    1.0335  0.3014   -1.3231   4.2748
## bin.temp15-20:HabitatBoth  2.2172  2.3707    0.9352  0.3497   -2.4293   6.8636
## bin.temp20-25:HabitatBoth  2.8733  2.4354    1.1798  0.2381   -1.9000   7.6466
## bin.temp25-30:HabitatBoth  3.7065  2.4500    1.5129  0.1303   -1.0954   8.5085
## bin.temp30-35:HabitatBoth  1.5092  2.4684    0.6114  0.5409   -3.3288   6.3473
## bin.temp35-40:HabitatBoth  3.6589  2.8362    1.2901  0.1970   -1.9000   9.2179
## bin.temp15-20:HabitatTerrestrial -1.4849  1.5504   -0.9577  0.3382   -4.5236   1.5539
## bin.temp20-25:HabitatTerrestrial -1.9079  1.6396   -1.1636  0.2446   -5.1215   1.3058
## bin.temp25-30:HabitatTerrestrial -0.1145  1.5314   -0.0748  0.9404   -3.1160   2.8870
## bin.temp30-35:HabitatTerrestrial -2.4610  1.7456   -1.4098  0.1586   -5.8823   0.9603
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```