Meta-Analysis for Survival: Summary Excluding HUM251

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1. Summary

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

2. Setup

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

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

allsurv <- rbind(survdata_warm, survdata_cool)

### select data for analysis
rdata <- allsurv

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.

```r
### 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.

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

```
## [1] 28
```

```r
nlevels(rdata$study_code)  # Check number of studies
```

```
## [1] 27
```

The final stage in the setup is to import a phylogentic 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_surv_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)
```
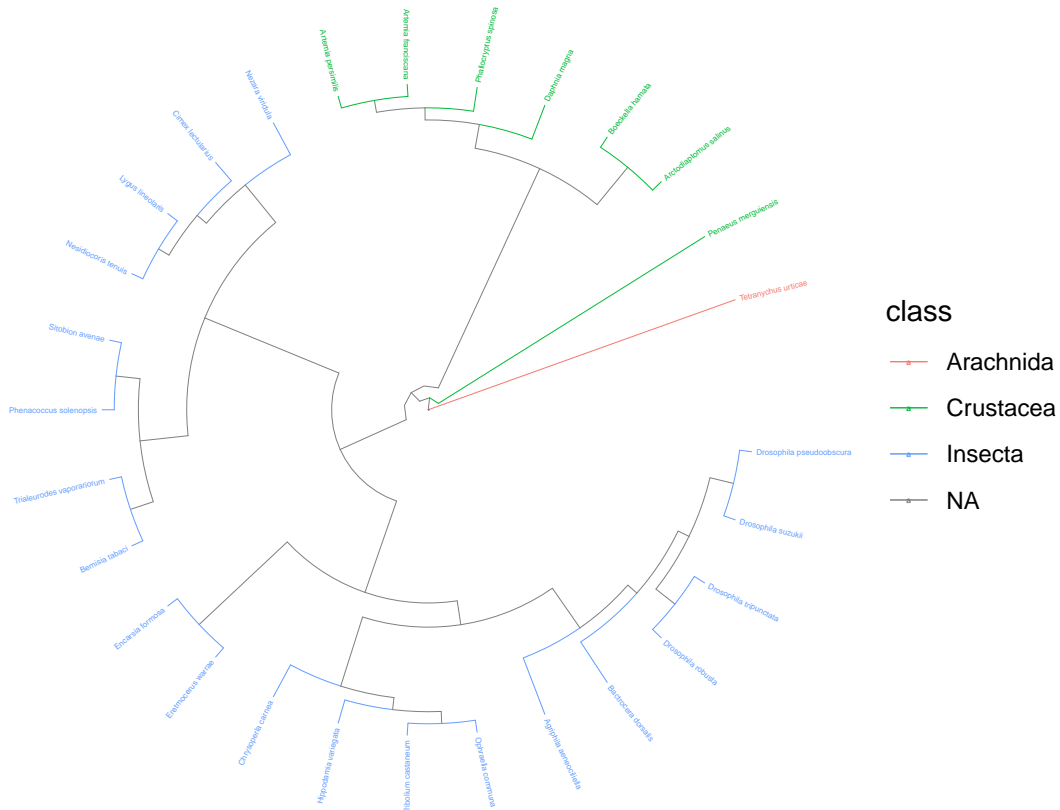
3. Random effects models

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.

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)
```

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 = 85; method: REML)
##
##      logLik   Deviance       AIC        BIC       AICc
## -349.9147   699.8294   709.8294   721.9835   710.5986
##
## Variance Components:
##
##               estim      sqrt   nlvls   fixed          factor
## sigma^2.1    0.0000    0.0002      28      no         species
## sigma^2.2   72.5143    8.5155      27      no      study_code
## sigma^2.3    0.0000    0.0005      36      no  shared_control
## sigma^2.4  140.7682   11.8646      85      no             obs
##
## Test for Heterogeneity:
## Q(df = 84) = 3938.4381, p-val < .0001
##
## Model Results:
##
## estimate       se      zval     pval     ci.lb    ci.ub
##  -3.0013   2.1940   -1.3680   0.1713   -7.3014   1.2988
##
## ---
## 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
##      9.998450e+01    2.805794e-08    3.399391e+01      1.293475e-07    6.599059e+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 = 85; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -349.9147   699.8294   707.8294   717.5527   708.3357
##
## Variance Components:
##
##               estim     sqrt   nlvls   fixed            factor
## sigma^2.1   72.5143   8.5155      27      no        study_code
## sigma^2.2    0.0000   0.0007      36      no   shared_control
## sigma^2.3  140.7682  11.8646      85      no               obs
##
## Test for Heterogeneity:
## Q(df = 84) = 3938.4381, p-val < .0001
##
## Model Results:
##
## estimate       se      zval     pval    ci.lb   ci.ub
##  -3.0013   2.1940   -1.3680   0.1713  -7.3014  1.2988
##
## ---
## 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
##       9.998450e+01     3.399391e+01      2.337164e-07    6.599059e+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 = 85; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -355.6983   711.3967   717.3967   724.6891   717.6967
##
## Variance Components:
##
##              estim      sqrt   nlvls  fixed          factor
## sigma^2.1   45.1593    6.7201      36     no  shared_control
## sigma^2.2  177.5153   13.3235      85     no             obs
##
## Test for Heterogeneity:
## Q(df = 84) = 3938.4381, p-val < .0001
##
## Model Results:
##
## estimate       se      zval      pval     ci.lb     ci.ub
##  -3.6051   1.9279   -1.8700    0.0615   -7.3837    0.1735  .
##
## ---
## 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
##           99.98516          20.27738          79.70778
```

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 = 85; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -349.9147   699.8294   705.8294   713.1218   706.1294
##
## Variance Components:
##
##              estim     sqrt  nlvls  fixed      factor
## sigma^2.1   72.5143   8.5155     27     no  study_code
## sigma^2.2  140.7682  11.8646     85     no         obs
##
## Test for Heterogeneity:
## Q(df = 84) = 3938.4381, p-val < .0001
##
## Model Results:
##
## estimate       se     zval     pval     ci.lb    ci.ub
##  -3.0013   2.1940  -1.3680   0.1713   -7.3014   1.2988
##
## ---
## 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
##      99.98450      33.99391    65.99059
```

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 (Δ 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, "meta8" 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 havea 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 = 85; method: REML)
##
##     logLik   Deviance       AIC        BIC       AICc
## -345.9459   691.8918   701.8918   713.9860   702.6711
##
## Variance Components:
##
##                estim     sqrt  nlvls  fixed          factor
## sigma^2.1    74.6180   8.6382     27     no      study_code
## sigma^2.2     0.0000   0.0007     36     no  shared_control
## sigma^2.3   142.5323  11.9387     85     no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 83) = 3456.0460, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 0.3754, p-val = 0.5401
##
## Model Results:
##
##            estimate       se     zval     pval      ci.lb     ci.ub
## intrcpt      2.4389   9.1576   0.2663   0.7900   -15.5097   20.3874
## reftemp     -0.2170   0.3542  -0.6127   0.5401    -0.9112    0.4772
##
## ---
## 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 = 85; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -344.9461   689.8921   699.8921   711.9863   700.6714
##
## Variance Components:
##
##               estim     sqrt  nlvls  fixed          factor
## sigma^2.1   71.1673   8.4361     27     no      study_code
## sigma^2.2    0.0000   0.0007     36     no  shared_control
## sigma^2.3  141.0916  11.8782     85     no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 83) = 3034.8408, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 2.3510, p-val = 0.1252
##
## Model Results:
##
##            estimate       se     zval     pval     ci.lb    ci.ub
## intrcpt    -10.7272   5.4890  -1.9543   0.0507  -21.4856   0.0311   .
## treattemp    0.2596   0.1693   1.5333   0.1252   -0.0722   0.5915
##
## ---
## 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 = 85; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -345.7413   691.4825   701.4825   713.5767   702.2618
##
## Variance Components:
##
##               estim     sqrt  nlvls  fixed          factor
## sigma^2.1   66.3047   8.1428     27     no      study_code
## sigma^2.2    0.0000   0.0006     36     no  shared_control
## sigma^2.3  145.3240  12.0550     85     no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 83) = 3734.1654, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 1.0442, p-val = 0.3068
##
## Model Results:
##
##               estimate       se     zval     pval     ci.lb     ci.ub
## intrcpt        -5.8138   3.4703  -1.6753   0.0939  -12.6155    0.9879  .
## warm.coolWarm   3.9541   3.8695   1.0219   0.3068   -3.6299   11.5381
##
## ---
## 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 = 85; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -343.5229   687.0459   697.0459   709.1401   697.8251
##
## Variance Components:
##
##                estim     sqrt  nlvls  fixed          factor
## sigma^2.1    61.4520   7.8391     27     no      study_code
## sigma^2.2     0.0000   0.0007     36     no  shared_control
## sigma^2.3   140.0830  11.8357     85     no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 83) = 3112.8828, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 5.3508, p-val = 0.0207
##
## Model Results:
##
##          estimate       se     zval     pval     ci.lb     ci.ub
## intrcpt   -5.2158   2.2945  -2.2731   0.0230   -9.7130   -0.7186  *
## diff       0.4673   0.2020   2.3132   0.0207    0.0714    0.8633  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Treatment temperature as a quadratic effect

We expect that treatment temperature will have a non-linear effect on survival We expect that the relationship will be quadratic. More specifically, we expect that survival will decrease at both extreme high and low temperatures. We also assume that th optimum survival temperature will be close to the control temperature. That said, we investigate **treattemp** as a quadratic fixed 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 = 85; method: REML)
##
##      logLik   Deviance        AIC        BIC       AICc
## -339.5005    679.0010   691.0010   705.4413   692.1210
##
## Variance Components:
##
##               estim     sqrt   nlvls   fixed          factor
## sigma^2.1    78.5394   8.8622      27      no      study_code
## sigma^2.2     0.0000   0.0006      36      no   shared_control
## sigma^2.3   132.9900  11.5321      85      no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 82) = 2260.0893, p-val < .0001
##
## Test of Moderators (coefficients 2:3):
## QM(df = 2) = 6.1357, p-val = 0.0465
##
## Model Results:
##
##                                      estimate       se      zval     pval      ci.lb     ci.ub
## intrcpt                              -24.5360   9.0005   -2.7261   0.0064   -42.1766   -6.8953   **
## poly(treattemp, degree = 2, raw = TRUE)1    1.5447   0.6802    2.2709   0.0232     0.2115    2.8779    *
## poly(treattemp, degree = 2, raw = TRUE)2   -0.0239   0.0122   -1.9521   0.0509    -0.0479    0.0001    .
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

For completeness we also investigate treatment temperature as a cubic 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 = 85; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -335.6332   671.2663   685.2663   702.0274   686.8006
##
## Variance Components:
##
##              estim     sqrt  nlvls  fixed           factor
## sigma^2.1   74.7206   8.6441     27     no        study_code
## sigma^2.2    0.0000   0.0007     36     no   shared_control
## sigma^2.3  136.5471  11.6853     85     no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 81) = 2247.3006, p-val < .0001
##
## Test of Moderators (coefficients 2:4):
## QM(df = 3) = 6.6153, p-val = 0.0852
##
## Model Results:
##
##                                       estimate        se     zval     pval      ci.lb    ci.ub
## intrcpt                               -17.4076   12.8696  -1.3526   0.1762   -42.6315   7.8164
## poly(treattemp, degree = 3, raw = TRUE)1    0.2948    1.7501   0.1685   0.8662    -3.1353   3.7250
## poly(treattemp, degree = 3, raw = TRUE)2    0.0305    0.0716   0.4256   0.6704    -0.1099   0.1708
## poly(treattemp, degree = 3, raw = TRUE)3   -0.0007    0.0009  -0.7662   0.4435    -0.0024   0.0011
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Below is a bubble plot of the fitted quadratic model.
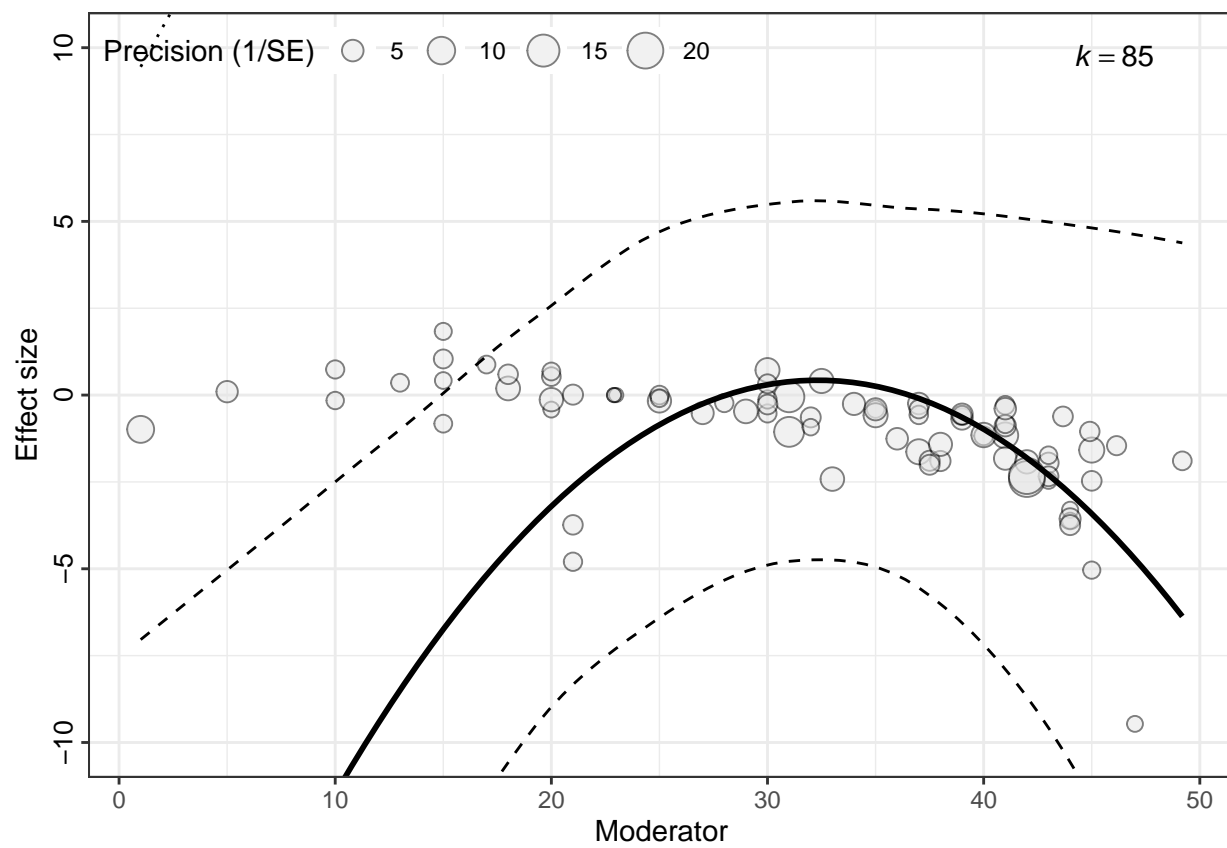
Modelling response with binned treatment temperatures

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
##     7    27     7    10     6    12    16
```

```
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 = 85; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -313.7994   627.5987   647.5987   671.1658   650.8823
##
## Variance Components:
##
##              estim      sqrt   nlvls   fixed          factor
## sigma^2.1   114.0443   10.6792      27      no       study_code
## sigma^2.2     0.0000    0.0006      36      no   shared_control
## sigma^2.3    91.8758    9.5852      85      no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 78) = 2524.1926, p-val < .0001
##
## Test of Moderators (coefficients 1:7):
## QM(df = 7) = 37.5741, p-val < .0001
##
## Model Results:
##
##                 estimate       se      zval     pval      ci.lb      ci.ub
## bin.temp<15     -27.0742   5.3249   -5.0845   <.0001   -37.5108   -16.6377   ***
## bin.temp>40      -1.9126   3.7319   -0.5125   0.6083    -9.2270     5.4018
## bin.temp15-20    -2.0967   4.7401   -0.4423   0.6582   -11.3870     7.1937
## bin.temp20-25     9.5915   4.5299    2.1174   0.0342     0.7131    18.4700     *
## bin.temp25-30    -4.9591   5.4400   -0.9116   0.3620   -15.6213     5.7031
## bin.temp30-35     0.0778   4.1952    0.0186   0.9852    -8.1447     8.3003
## bin.temp35-40    -0.2971   3.9107   -0.0760   0.9395    -7.9619     7.3678
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
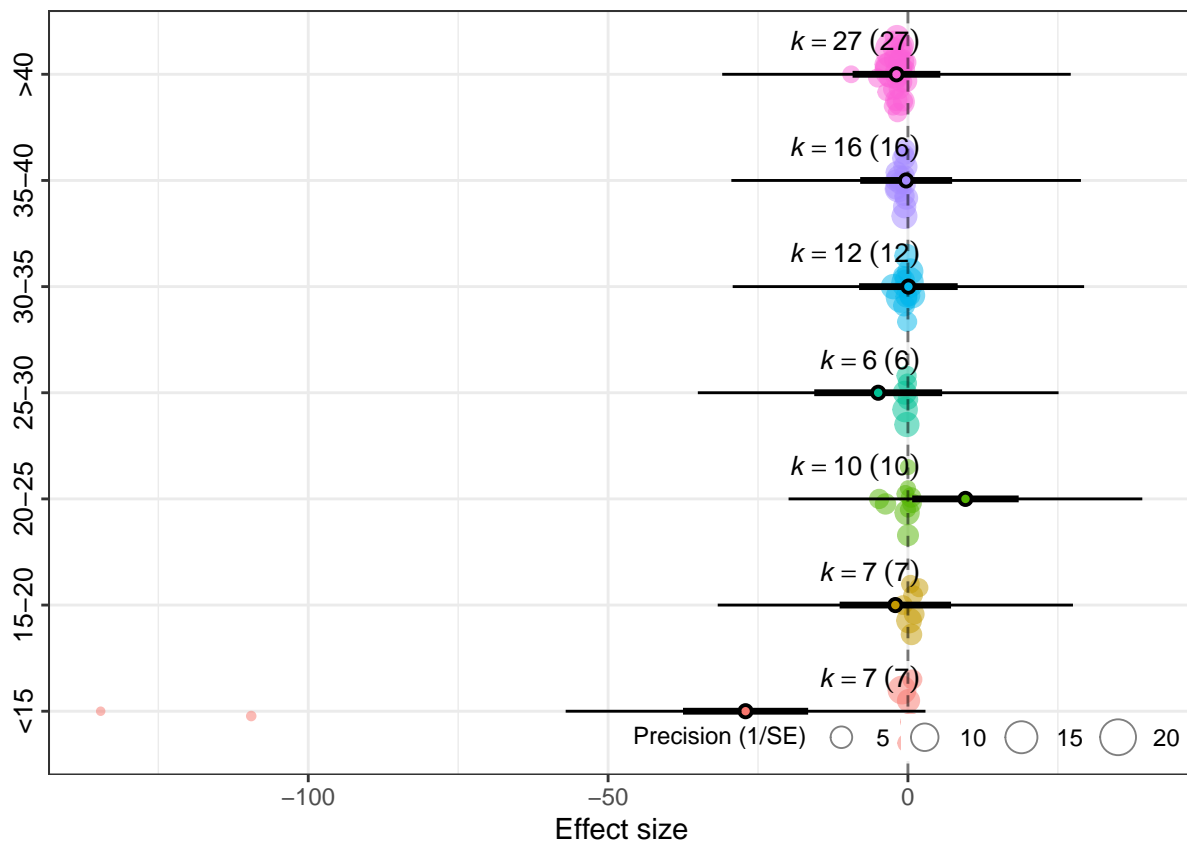
The two extremely outlying points in the <15 category are both from the study OSM205. We will investigate the removal of these outlying points later.

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 = 85; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -345.9752   691.9503   701.9503   714.0445   702.7295
##
## Variance Components:
##
##                 estim     sqrt  nlvls  fixed          factor
## sigma^2.1     74.7425   8.6454     27     no      study_code
## sigma^2.2      0.0000   0.0010     36     no  shared_control
## sigma^2.3    142.8900  11.9537     85     no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 83) = 3368.5188, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 0.2882, p-val = 0.5914
##
## Model Results:
##
##                   estimate        se     zval    pval       ci.lb      ci.ub
## intrcpt          -303.5085  559.7274  -0.5422  0.5877  -1400.5539   793.5370
## Publication.year    0.1493    0.2782   0.5369  0.5914     -0.3958     0.6945
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

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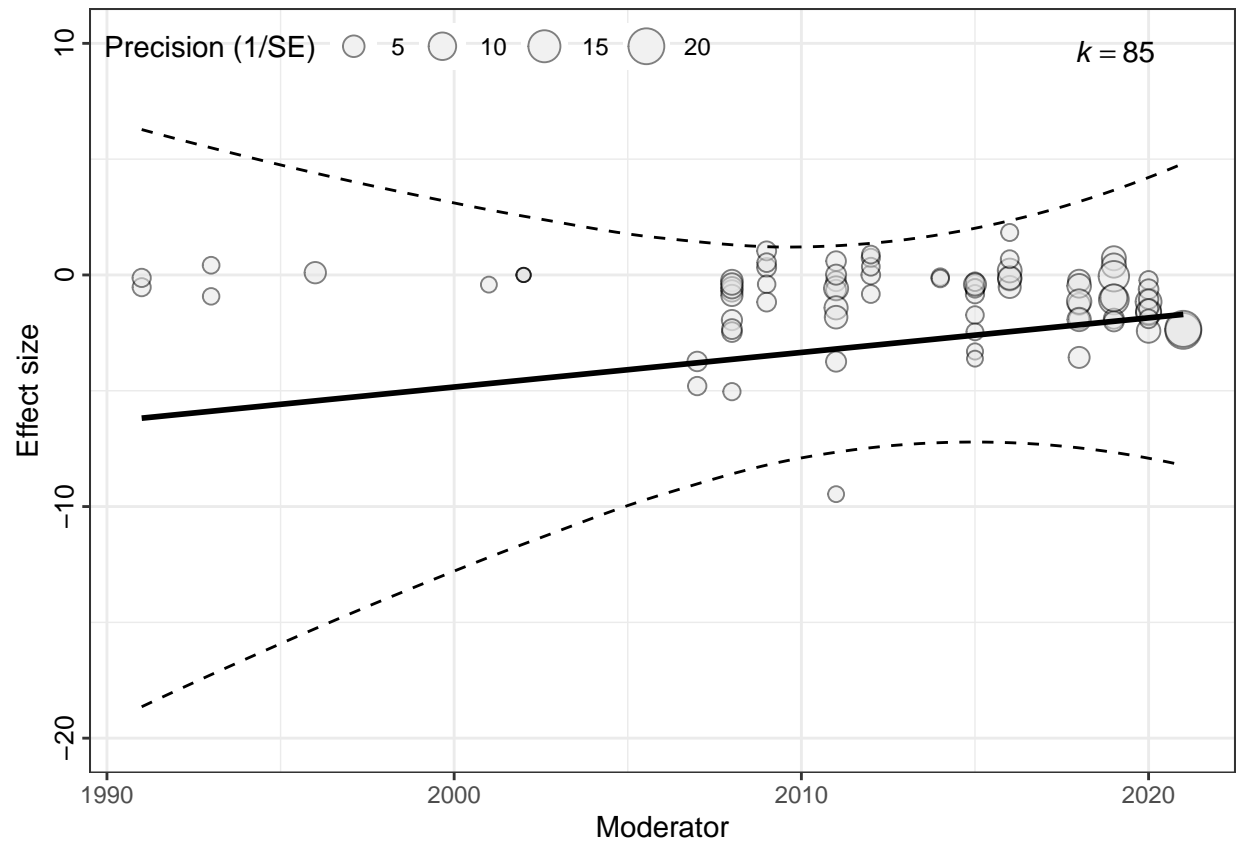
Sensitivity Analysis

What happens when we remove OSM205, which is clearly an outlying effect size.

```
rdata_exc205 <- subset(rdata, Paper.code != "OSM205")
new_vcv <- impute_covariance_matrix(vi = rdata_exc205$v, cluster = rdata_exc205$shared_control,
    r = 0.5)
```

Treatment temperature

```
meta_trait_treattemp_new <- rma.mv(es, new_vcv, mod = ~treattemp,
    random = list(~1 | study_code, ~1 | shared_control, ~1 |
        obs), data = rdata_exc205, method = "REML")
```

```
summary(meta_trait_treattemp_new)
```

```
##
## Multivariate Meta-Analysis Model (k = 81; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -125.1489   250.2978   260.2978   272.1450   261.1197
##
## Variance Components:
##
##              estim    sqrt  nlvls  fixed          factor
## sigma^2.1   0.0517  0.2274     26     no      study_code
## sigma^2.2   0.0000  0.0001     34     no  shared_control
## sigma^2.3   1.1798  1.0862     81     no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 79) = 2465.4918, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 44.4554, p-val < .0001
##
## Model Results:
##
##            estimate      se     zval    pval    ci.lb    ci.ub
## intrcpt      1.7287  0.4192   4.1240  <.0001   0.9071   2.5503  ***
## treattemp   -0.0824  0.0124  -6.6675  <.0001  -0.1067  -0.0582  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Warm vs Cool

```
meta_trait_warm_new <- rma.mv(es, new_vcv, mod = ~warm.cool,
    random = list(~1 | study_code, ~1 | shared_control, ~1 |
        obs), data = rdata_exc205, method = "REML")
```

```
summary(meta_trait_warm_new)
```

```
##
## Multivariate Meta-Analysis Model (k = 81; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -135.5184   271.0367   281.0367   292.8840   281.8586
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed           factor
## sigma^2.1  0.1682  0.4102     26     no       study_code
## sigma^2.2  0.0000  0.0001     34     no   shared_control
## sigma^2.3  1.4978  1.2238     81     no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 79) = 3176.4269, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 13.8714, p-val = 0.0002
##
## Model Results:
##
##               estimate      se     zval    pval    ci.lb    ci.ub
## intrcpt         0.1657  0.3281   0.5049  0.6136  -0.4774   0.8088
## warm.coolWarm  -1.3736  0.3688  -3.7244  0.0002  -2.0965  -0.6508  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Difference

```
meta_trait_diff_new <- rma.mv(es, new_vcv, mod = ~diff, random = list(~1 |
    study_code, ~1 | shared_control, ~1 | obs), data = rdata_exc205,
    method = "REML")
```

```
summary(meta_trait_diff_new)
```
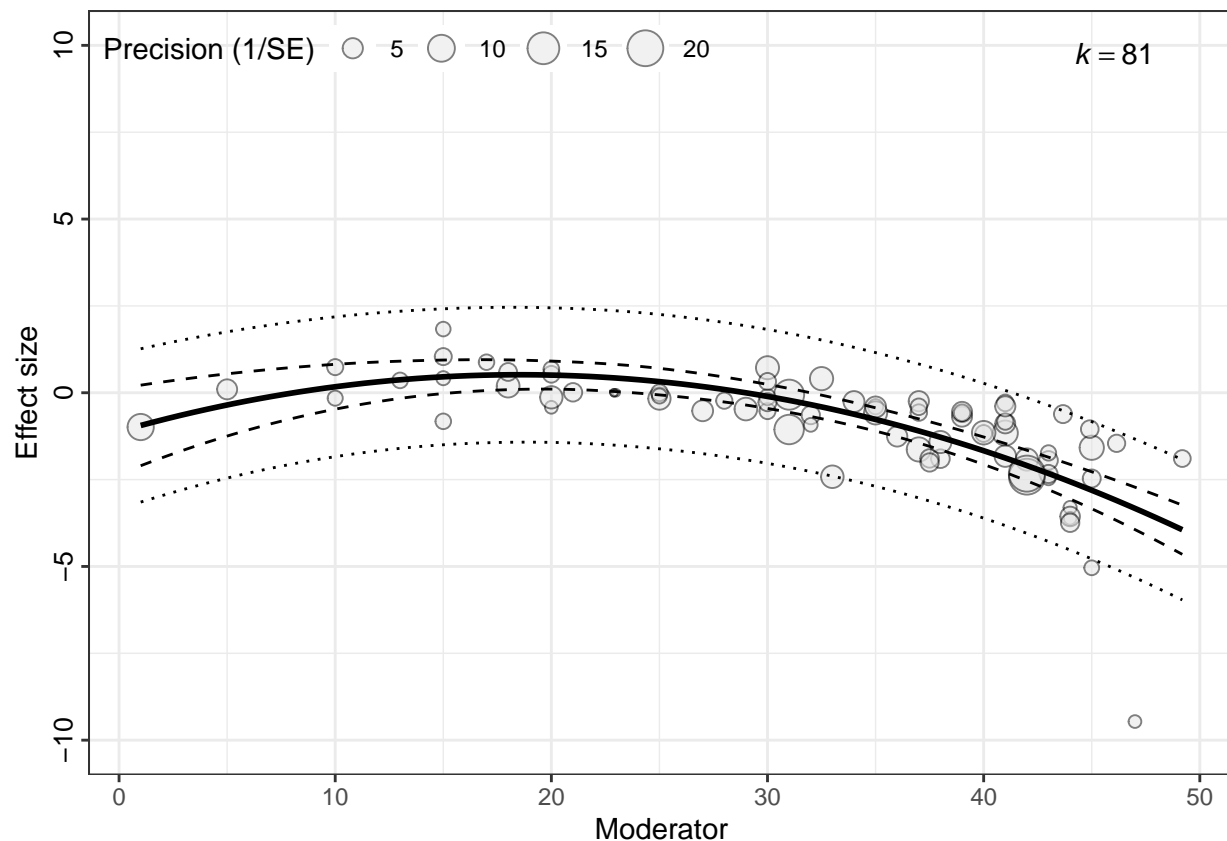
```
##
## Multivariate Meta-Analysis Model (k = 81; method: REML)
##
##    logLik   Deviance        AIC        BIC        AICc
## -122.8613   245.7226   255.7226   267.5698   256.5445
##
## Variance Components:
##
##            estim    sqrt   nlvls   fixed          factor
## sigma^2.1  0.1083  0.3291     26      no      study_code
## sigma^2.2  0.0000  0.0001     34      no  shared_control
## sigma^2.3  1.0661  1.0325     81      no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 79) = 2476.4162, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 48.3412, p-val < .0001
##
## Model Results:
##
##          estimate      se     zval     pval    ci.lb    ci.ub
## intrcpt   -0.1751  0.1767  -0.9911   0.3216  -0.5214   0.1712
## diff      -0.1125  0.0162  -6.9528  <.0001  -0.1442  -0.0808  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Treatment temperature as a quadratic effect

```
meta_trait_treat2_new <- rma.mv(es, new_vcv, mod = ~poly(treattemp,
    degree = 2, raw = TRUE), random = list(~1 | study_code, ~1 |
    shared_control, ~1 | obs), data = rdata_exc205, method = "REML")
```

```
summary(meta_trait_treat2_new)
```

```
##
## Multivariate Meta-Analysis Model (k = 81; method: REML)
##
##      logLik   Deviance        AIC        BIC       AICc
## -112.1996   224.3991   236.3991   250.5394   237.5822
##
## Variance Components:
##
##              estim     sqrt  nlvls  fixed          factor
## sigma^2.1   0.1753   0.4187     26     no      study_code
## sigma^2.2   0.0000   0.0001     34     no  shared_control
## sigma^2.3   0.7609   0.8723     81     no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 78) = 1625.7038, p-val < .0001
##
## Test of Moderators (coefficients 2:3):
## QM(df = 2) = 77.9784, p-val < .0001
##
## Model Results:
##
##                                      estimate      se     zval    pval    ci.lb    ci.ub
## intrcpt                               -1.1125  0.6527  -1.7045  0.0883  -2.3917   0.1668      .
## poly(treattemp, degree = 2, raw = TRUE)1    0.1760  0.0491   3.5835  0.0003   0.0797   0.2723  ***
## poly(treattemp, degree = 2, raw = TRUE)2   -0.0047  0.0009  -5.4094  <.0001  -0.0065  -0.0030  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Binned temperatures

```
meta_trait_bintemp_new <- rma.mv(es, new_vcv, mod = ~bin.temp -
    1, random = list(~1 | study_code, ~1 | shared_control, ~1 |
    obs), data = rdata_exc205, method = "REML")
summary(meta_trait_bintemp_new)
```

```
##
## Multivariate Meta-Analysis Model (k = 81; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -116.4513   232.9025   252.9025   275.9432   256.3946
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed           factor
## sigma^2.1  0.0338  0.1839     26     no       study_code
## sigma^2.2  0.0000  0.0001     34     no   shared_control
## sigma^2.3  1.1591  1.0766     81     no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 74) = 1945.9037, p-val < .0001
##
## Test of Moderators (coefficients 1:7):
## QM(df = 7) = 98.6003, p-val < .0001
##
```

```
## Model Results:
##
##                estimate      se     zval    pval    ci.lb    ci.ub
## bin.temp<15      0.0020  0.5111   0.0040  0.9968  -0.9997   1.0038
## bin.temp>40     -2.1939  0.2318  -9.4651  <.0001  -2.6481  -1.7396   ***
## bin.temp15-20    0.5513  0.4351   1.2671  0.2051  -0.3015   1.4040
## bin.temp20-25    0.0698  0.4305   0.1621  0.8712  -0.7740   0.9136
## bin.temp25-30   -0.2402  0.4616  -0.5205  0.6027  -1.1449   0.6645
## bin.temp30-35   -0.4131  0.3269  -1.2637  0.2063  -1.0537   0.2276
## bin.temp35-40   -0.9175  0.2862  -3.2053  0.0013  -1.4786  -0.3565    **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
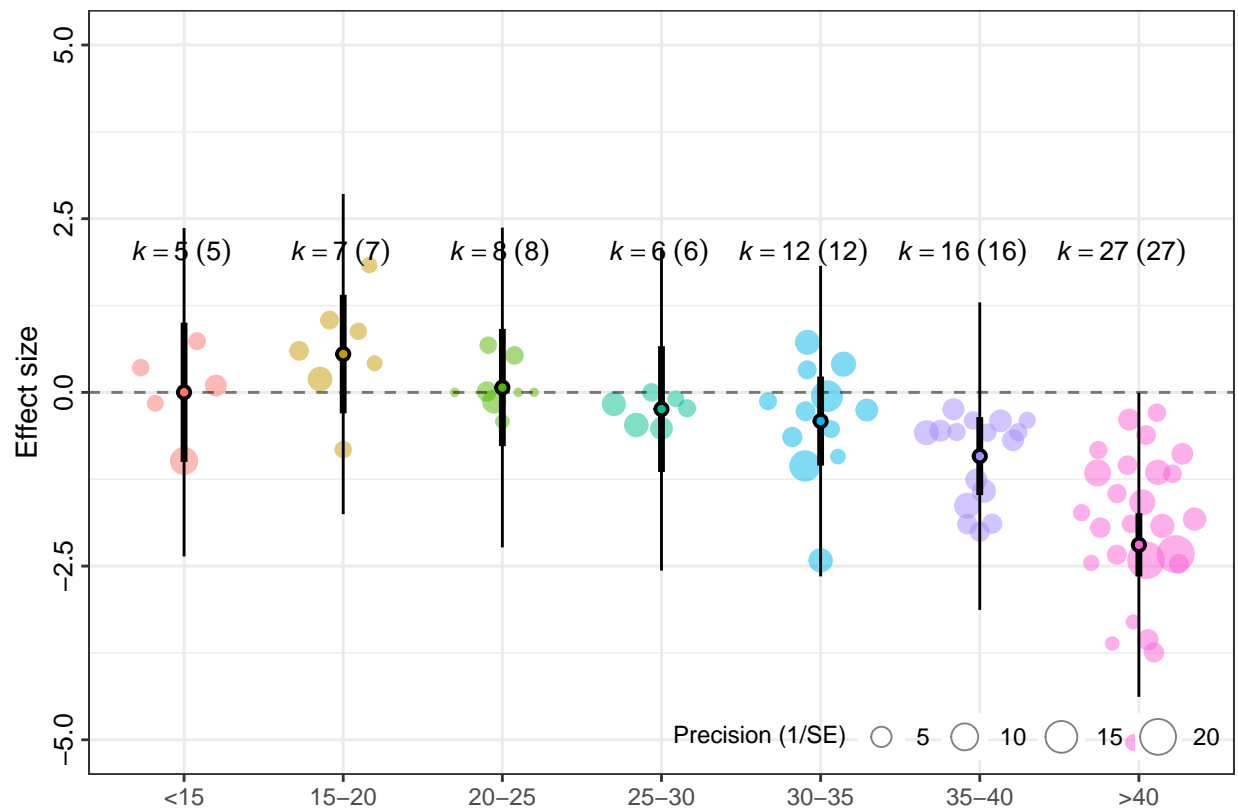
Sensitivty Analysis

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%
## -9.021988
```

```
print(maxq)
```

```
##      97.5%
## 0.8650332
```

We run the quadratic 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 quadratic effect (sesnsitivity analysis)

We re-create the variance-covariance matrix with our new substted 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)
```
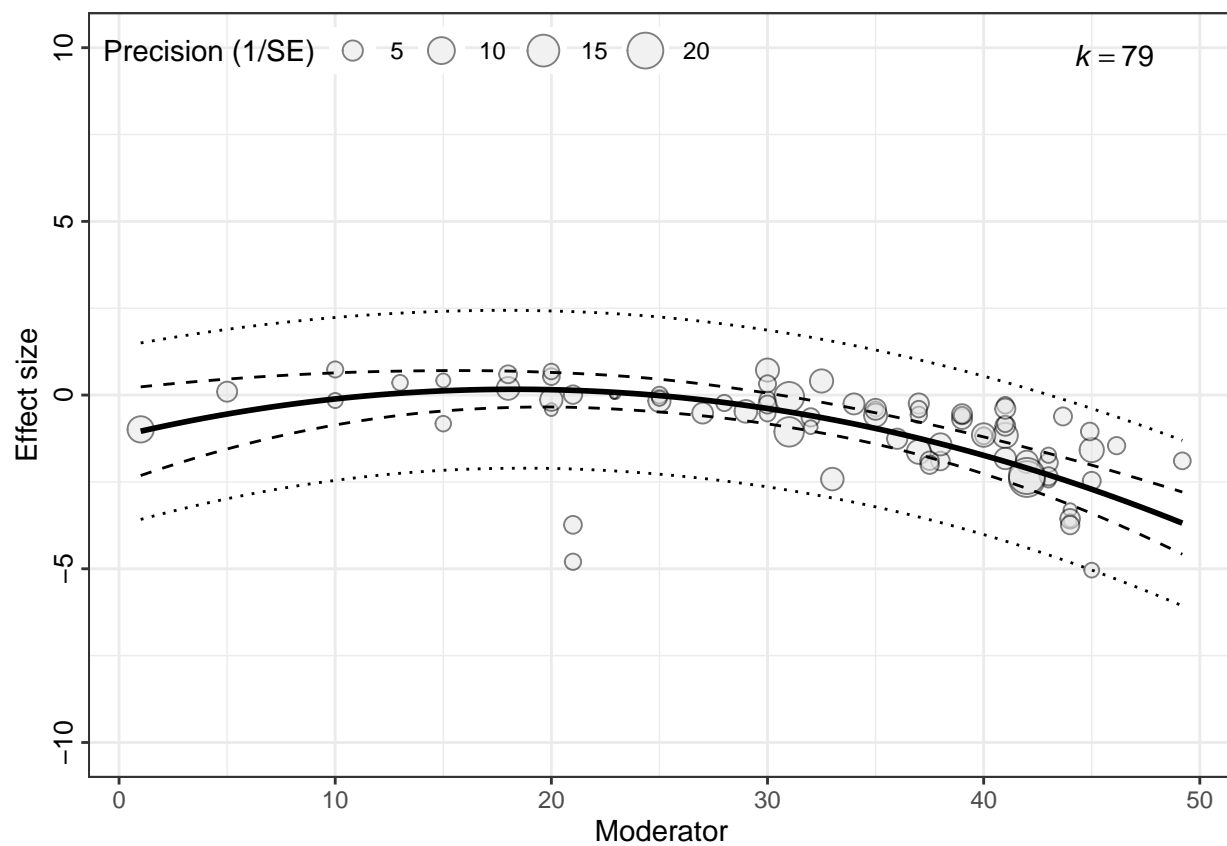
```
meta_sa_treat2 <- rma.mv(es, VCV_shared_sa, mod = ~poly(treattemp,
    degree = 2, raw = TRUE), random = list(~1 | study_code, ~1 |
    shared_control, ~1 | obs), data = sdata, method = "REML")
```

```
summary(meta_sa_treat2)
```

```
##
## Multivariate Meta-Analysis Model (k = 79; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -104.5365   209.0730   221.0730   235.0574   222.2904
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed          factor
## sigma^2.1  0.7816  0.8841     27     no       study_code
## sigma^2.2  0.0000  0.0000     36     no   shared_control
## sigma^2.3  0.4934  0.7024     79     no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 76) = 1807.3647, p-val < .0001
##
## Test of Moderators (coefficients 2:3):
## QM(df = 2) = 41.3201, p-val < .0001
##
## Model Results:
##
##                                     estimate      se     zval    pval    ci.lb    ci.ub
## intrcpt                             -1.1830  0.7153  -1.6539  0.0981  -2.5850   0.2189     .
## poly(treattemp, degree = 2, raw = TRUE)1   0.1476  0.0523   2.8206  0.0048   0.0450   0.2502   **
```

```
## poly(treattemp, degree = 2, raw = TRUE)2   -0.0040  0.0009  -4.2838  <.0001  -0.0059  -0.0022  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

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

Modelling temperature as a linear fixed effect (Sensitivity analysis)

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

```
summary(meta_sa_treat)
```

```
##
## Multivariate Meta-Analysis Model (k = 79; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -113.4144   226.8289   236.8289   248.5479   237.6739
##
## Variance Components:
##
##              estim     sqrt   nlvls   fixed          factor
## sigma^2.1   0.6001   0.7747      27      no      study_code
## sigma^2.2   0.0000   0.0000      36      no   shared_control
## sigma^2.3   0.7046   0.8394      79      no             obs
##
## Test for Residual Heterogeneity:
## QE(df = 77) = 2451.9964, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 18.3972, p-val < .0001
##
## Model Results:
##
##             estimate       se     zval     pval    ci.lb    ci.ub
## intrcpt       0.9963   0.4812   2.0705   0.0384   0.0532   1.9394     *
## treattemp    -0.0631   0.0147  -4.2892  <.0001  -0.0920  -0.0343   ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Below is a bubble plot of the fitted linear model to the subsetted data.
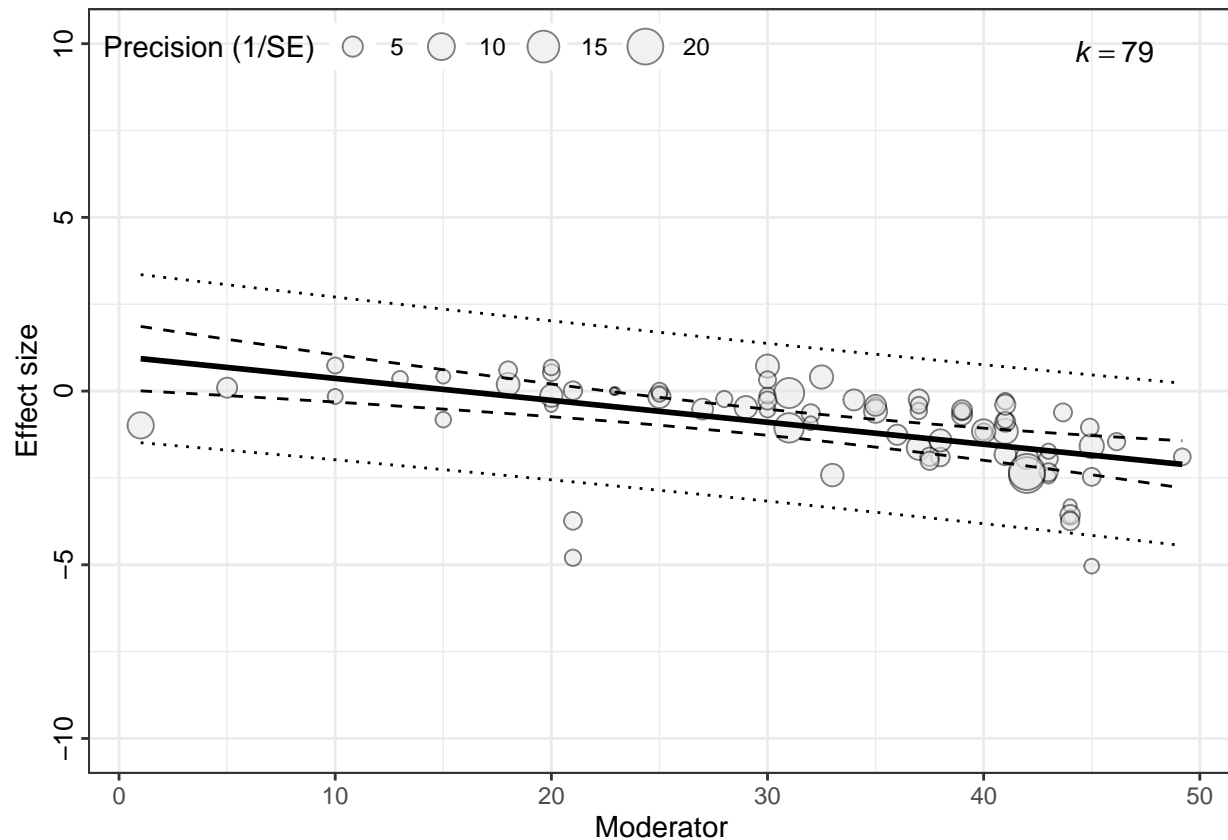
Modelling response with binned treatment temperatures

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
##     5    26     4    10     6    12    16
```

```
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 = 79; method: REML)
##
##    logLik  Deviance       AIC       BIC      AICc
## -105.0570  210.1140  230.1140  252.8806  233.7205
##
## Variance Components:
##
```

```
##               estim    sqrt  nlvls  fixed            factor
## sigma^2.1   0.4088  0.6394     27    no        study_code
## sigma^2.2   0.0000  0.0000     36    no    shared_control
## sigma^2.3   0.7561  0.8696     79    no               obs
##
## Test for Residual Heterogeneity:
## QE(df = 72) = 1983.1114, p-val < .0001
##
## Test of Moderators (coefficients 1:7):
## QM(df = 7) = 55.0410, p-val < .0001
##
## Model Results:
##
##                  estimate      se     zval    pval   ci.lb    ci.ub
## bin.temp<15        0.0262  0.5022   0.0522  0.9583  -0.9581   1.0106
## bin.temp>40       -2.0095  0.2810  -7.1515  <.0001  -2.5602  -1.4587   ***
## bin.temp15-20     -0.0419  0.5188  -0.0808  0.9356  -1.0588   0.9750
## bin.temp20-25     -0.7448  0.3846  -1.9364  0.0528  -1.4987   0.0090    .
## bin.temp25-30     -0.3084  0.4512  -0.6835  0.4943  -1.1928   0.5760
## bin.temp30-35     -0.5924  0.3348  -1.7694  0.0768  -1.2486   0.0638    .
## bin.temp35-40     -0.8907  0.3042  -2.9285  0.0034  -1.4868  -0.2946   **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```