

Meta-Analysis Reproduction Summary Excluding HUM251

Fay Frost

1. Summary

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

2. Setup

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

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

allrep <- rbind(repdata_warm, repdata_cool)

### select data for analysis
rdata <- allrep
```

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] 307

nlevels(rdata$study_code) # Check number of studies

## [1] 340
```

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_reproduction_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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -4121.5340    8243.0680    8253.0680    8279.3706    8253.1103
##
## Variance Components:
##
##      estim      sqrt nlvls  fixed      factor      R
## sigma^2.1  0.0000  0.0000   307    no Species.phylo  yes
## sigma^2.2  0.0000  0.0004   307    no      species    no
## sigma^2.3 10.2851  3.2070   340    no  study_code    no
## sigma^2.4  5.0427  2.2456  1424    no      obs      no
##
## Test for Heterogeneity:
## Q(df = 1423) = 37708.0554, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -1.5438  0.1885  -8.1879  <.0001  -1.9133  -1.1742  ***
##
## ---
## 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
##      9.945064e+01      3.871138e-10      9.206720e-07      6.673242e+01      3.271822e+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 <- matrix(0, nrow = dim(rdata)[1], ncol = dim(rdata)[1])
rownames(VCV_shared) <- rdata[, "es"]
colnames(VCV_shared) <- rdata[, "es"]
shared_coord <- which(rdata[, "shared_control"] %in% rdata[duplicated(rdata[,
  "shared_control"]), "shared_control"] == TRUE)
```

```

# Finds effect sizes that share a control group
combinations <- do.call("rbind", tapply(shared_coord, rdata[shared_coord,
  "shared_control"], function(x) t(utils::combn(x, 2))))
for (i in 1:dim(combinations)[1]) {
  p1 <- combinations[i, 1]
  p2 <- combinations[i, 2]
  p1_p2_cov <- 0.5 * sqrt(rdata[p1, "v"]) * sqrt(rdata[p2,
    "v"])
  VCV_shared[p1, p2] <- p1_p2_cov
  VCV_shared[p2, p1] <- p1_p2_cov
} # Calculates the covariance between effect sizes and enters them in each
# combination of coordinates
diag(VCV_shared) <- rdata[, "v"]
# Enters recalculated effect size sampling variances into
# diagonals

```

```

# 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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3840.3693    7680.7387    7692.7387    7724.3018    7692.7980
##
## Variance Components:
##
##      estim      sqrt      nlvls      fixed      factor      R
## sigma^2.1  0.0000  0.0000    307      no    Species.phylo  yes
## sigma^2.2  0.0000  0.0002    307      no      species      no
## sigma^2.3  5.0912  2.2564    340      no    study_code      no
## sigma^2.4  0.0000  0.0002    468      no  shared_control      no
## sigma^2.5  4.3173  2.0778   1424      no      obs      no
##
## Test for Heterogeneity:
## Q(df = 1423) = 39441.0068, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -1.3312  0.1399  -9.5141  <.0001  -1.6054  -1.0569  ***
##
## ---
## 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
##      9.910809e+01      2.151919e-09      4.290520e-07      5.362982e+01      4.308793e-07      4.547

```

Model without phylogeny

We also originally included a variance-covariance matrix for phylogenetic relatedness of the included species as a random effect in the model (Chamberlain et al., 2012), but this has now been removed 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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3840.3693    7680.7387    7690.7387    7717.0413    7690.7810
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.0000  0.0000   307    no      species
## sigma^2.2  5.0912  2.2564   340    no      study_code
## sigma^2.3  0.0000  0.0003   468    no      shared_control
## sigma^2.4  4.3173  2.0778  1424    no      obs
##
## Test for Heterogeneity:
## Q(df = 1423) = 39441.0068, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -1.3312  0.1399  -9.5141  <.0001  -1.6054  -1.0569  ***
##
## ---
## 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
##      9.910809e+01      2.623385e-08      5.362982e+01      9.228074e-07      4.547827e+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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3840.3693    7680.7387    7688.7387    7709.7808    7688.7669
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  5.0912  2.2564   340     no      study_code
## sigma^2.2  0.0000  0.0003   468     no    shared_control
## sigma^2.3  4.3173  2.0778  1424     no          obs
##
## Test for Heterogeneity:
## Q(df = 1423) = 39441.0068, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -1.3312  0.1399  -9.5141  <.0001  -1.6054  -1.0569  ***
##
## ---
## 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
##      9.910809e+01      5.362982e+01      9.202345e-07      4.547827e+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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3903.6019    7807.2038    7813.2038    7828.9854    7813.2207
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  3.7943  1.9479    468      no  shared_control
## sigma^2.2  4.4928  2.1196   1424      no              obs
##
## Test for Heterogeneity:
## Q(df = 1423) = 39441.0068, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -1.2616  0.1113 -11.3313 <.0001  -1.4798  -1.0434 ***
##
## ---
## 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
##      98.98863      45.32240      53.66623
```

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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3840.3693    7680.7387    7686.7387    7702.5203    7686.7556
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  5.0912  2.2564   340     no  study_code
## sigma^2.2  4.3173  2.0778  1424     no      obs
##
## Test for Heterogeneity:
## Q(df = 1423) = 39441.0068, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
## -1.3312  0.1399  -9.5141  <.0001  -1.6054  -1.0569  ***
##
## ---
## 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
##      99.10809      53.62982      45.47827
```

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 (< 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
- **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 = 1424; method: REML)  
##  
##      logLik      Deviance      AIC      BIC      AICc  
## -3837.1092    7674.2185    7684.2185    7710.5176    7684.2608  
##  
## Variance Components:  
##  
##      estim      sqrt  nlvls  fixed      factor  
## sigma^2.1  5.0470  2.2466   340     no    study_code  
## sigma^2.2  0.0000  0.0003   468     no  shared_control  
## sigma^2.3  4.3273  2.0802  1424     no           obs  
##  
## Test for Residual Heterogeneity:  
## QE(df = 1422) = 39267.0436, p-val < .0001  
##  
## Test of Moderators (coefficient 2):  
## QM(df = 1) = 1.6302, p-val = 0.2017  
##  
## Model Results:  
##  
##      estimate      se      zval      pval      ci.lb      ci.ub  
## intrcpt      0.1214  1.1461   0.1059  0.9157   -2.1249   2.3677  
## reftemp     -0.0588  0.0461  -1.2768  0.2017   -0.1491   0.0315  
##  
## ---  
## 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 = 1424; method: REML)  
##  
##      logLik      Deviance      AIC      BIC      AICc  
## -3829.9637    7659.9274    7669.9274    7696.2265    7669.9698  
##  
## Variance Components:  
##  
##      estim      sqrt  nlvls  fixed      factor  
## sigma^2.1  5.1024  2.2589   340     no      study_code  
## sigma^2.2  0.0000  0.0004   468     no  shared_control  
## sigma^2.3  4.2399  2.0591  1424     no          obs  
##  
## Test for Residual Heterogeneity:  
## QE(df = 1422) = 39393.9945, p-val < .0001  
##  
## Test of Moderators (coefficient 2):  
## QM(df = 1) = 17.0710, p-val < .0001  
##  
## Model Results:  
##  
##      estimate      se      zval      pval      ci.lb      ci.ub  
## intrcpt      -0.4750  0.2495  -1.9039  0.0569  -0.9640  0.0140  
## treattemp     -0.0349  0.0085  -4.1317  <.0001  -0.0515  -0.0184 ***  
##  
## ---  
## 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 = 1424; method: REML)  
##  
##      logLik      Deviance      AIC      BIC      AICc  
## -3830.7624    7661.5249    7671.5249    7697.8240    7671.5673  
##  
## Variance Components:  
##  
##      estim      sqrt  nlvls  fixed      factor  
## sigma^2.1  5.0827  2.2545   340     no      study_code  
## sigma^2.2  0.0000  0.0003   468     no  shared_control  
## sigma^2.3  4.2465  2.0607  1424     no              obs  
##  
## Test for Residual Heterogeneity:  
## QE(df = 1422) = 39147.9651, p-val < .0001  
##  
## Test of Moderators (coefficient 2):  
## QM(df = 1) = 15.7202, p-val < .0001  
##  
## Model Results:  
##  
##      estimate      se      zval      pval      ci.lb      ci.ub  
## intrcpt      -1.0716  0.1539  -6.9619  <.0001  -1.3733  -0.7699  ***  
## warm.coolWarm  -0.5069  0.1278  -3.9649  <.0001  -0.7575  -0.2563  ***  
##  
## ---  
## 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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3830.7624   7661.5249   7671.5249   7697.8240   7671.5673
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  5.0827  2.2545   340    no      study_code
## sigma^2.2  0.0000  0.0003   468    no  shared_control
## sigma^2.3  4.2465  2.0607  1424    no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 1422) = 39147.9651, p-val < .0001
##
## Test of Moderators (coefficients 1:2):
## QM(df = 2) = 106.3391, p-val < .0001
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## warm.coolCool   -1.0716  0.1539   -6.9619  <.0001   -1.3733   -0.7699  ***
## warm.coolWarm   -1.5785  0.1531  -10.3077  <.0001   -1.8787   -1.2784  ***
##
## ---
## 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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3830.6590    7661.3181    7671.3181    7697.6172    7671.3604
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  5.1557  2.2706   340     no      study_code
## sigma^2.2  0.0000  0.0003   468     no      shared_control
## sigma^2.3  4.2353  2.0580  1424     no          obs
##
## Test for Residual Heterogeneity:
## QE(df = 1422) = 39332.0046, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 15.7337, p-val < .0001
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt    -1.3371  0.1404  -9.5267  <.0001   -1.6122   -1.0620 ***
## diff        -0.0340  0.0086  -3.9666  <.0001   -0.0509   -0.0172 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Treatment temperature as a quadratic effect

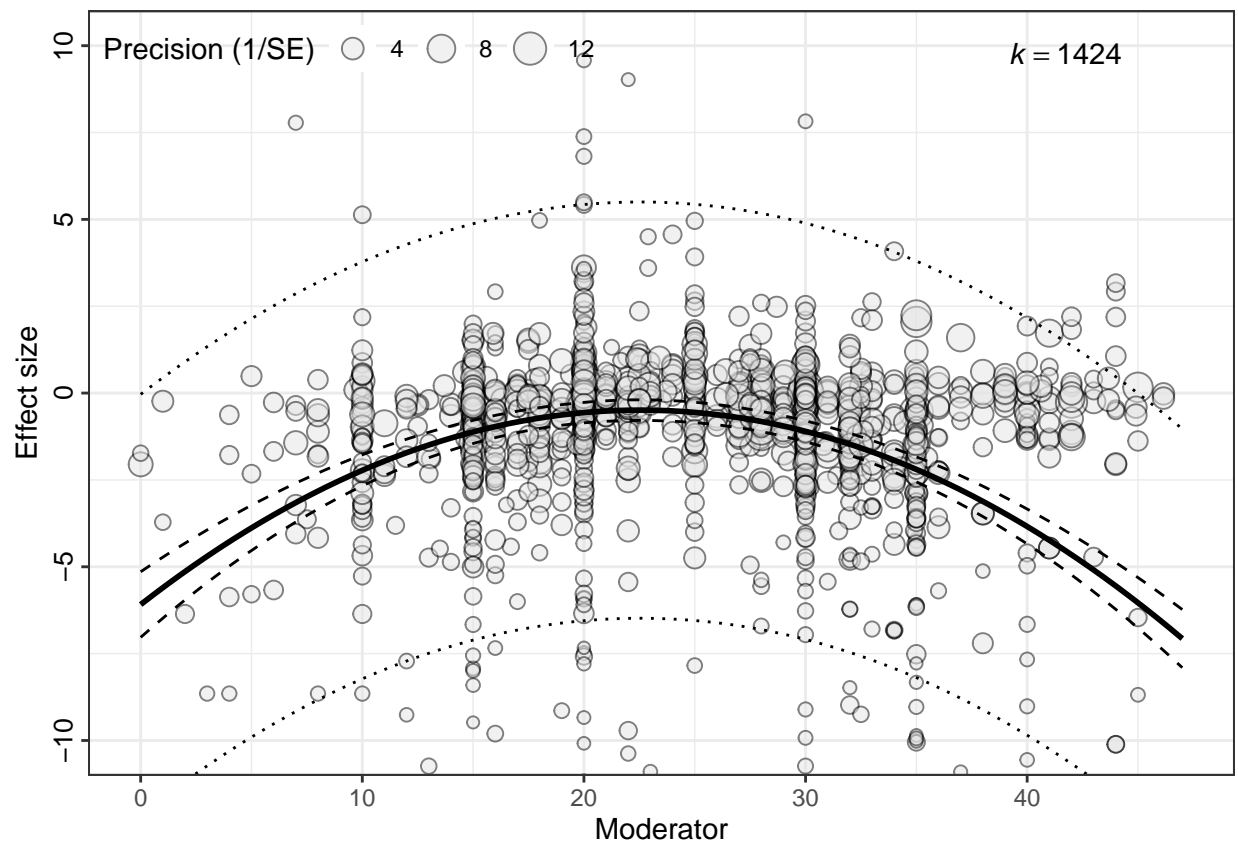
We expect that treatment temperature will have a quadratic effect on reproduction. In other words, we expect that reproduction will decrease either side of an optimum temperature for each species. We also assume that this optimum temperature will be close to the control temperature. That said, we investigate **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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3751.6511    7503.3022    7515.3022    7546.8569    7515.3616
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  5.7558  2.3991   340     no      study_code
## sigma^2.2  0.0548  0.2342   468     no  shared_control
## sigma^2.3  3.5092  1.8733  1424     no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 1421) = 37369.1059, p-val < .0001
##
## Test of Moderators (coefficients 2:3):
## QM(df = 2) = 188.2145, p-val < .0001
##
## Model Results:
##
##              estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt              -6.0870  0.4969  -12.2510 <.0001    -7.0608   -5.1132 ***
## poly(treattemp, degree = 2, raw = TRUE)1    0.4963  0.0417   11.8897 <.0001     0.4145    0.5782 ***
## poly(treattemp, degree = 2, raw = TRUE)2   -0.0110  0.0008  -12.9639 <.0001    -0.0127   -0.0093 ***
##
## ---
## 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

```
## [1] "<15" ">40" "15-20" "20-25" "25-30" "30-35" "35-40"
```

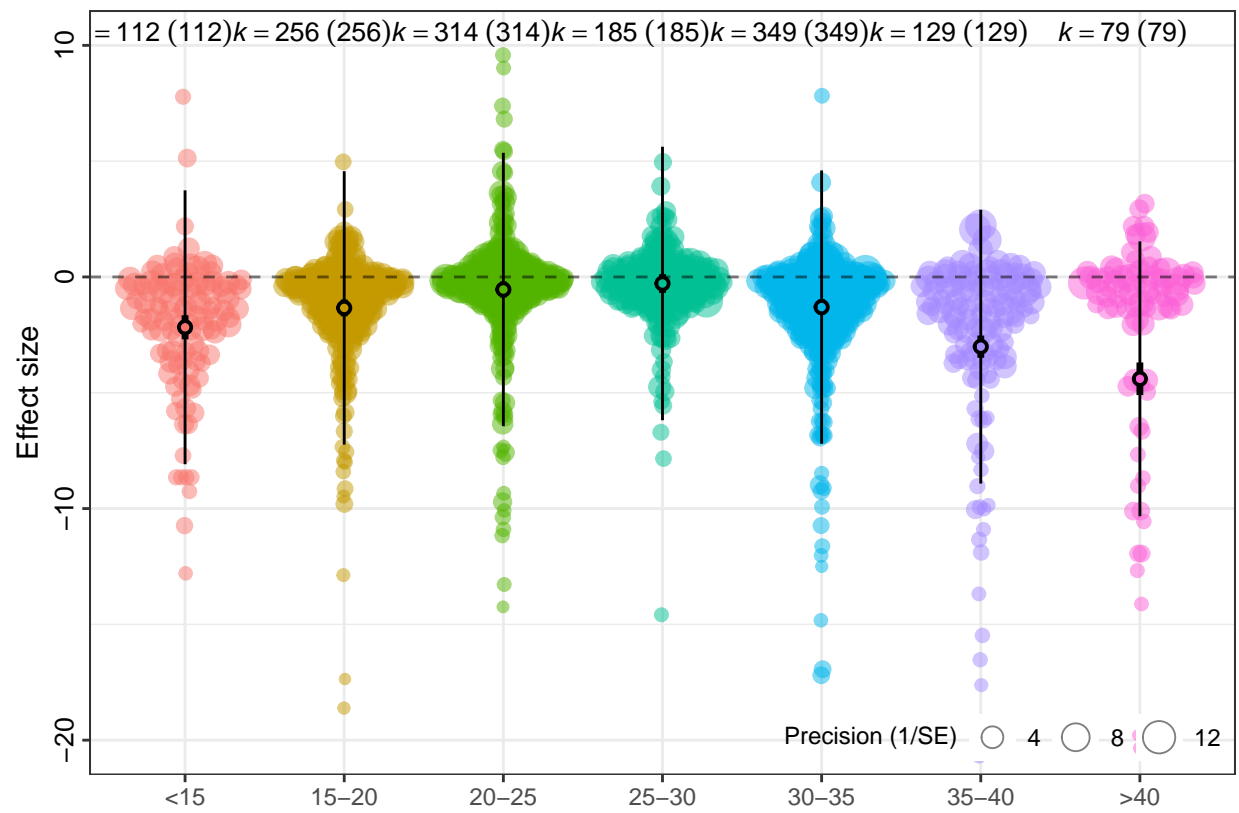
```
table(rdata$bin.temp)
```

```
##
##    <15    >40  15-20  20-25  25-30  30-35  35-40
##    112     79   256    314   185    349   129
```

```
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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3733.0491    7466.0982    7486.0982    7538.6612    7486.2547
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  5.5172  2.3489   340     no      study_code
## sigma^2.2  0.0083  0.0910   468     no  shared_control
## sigma^2.3  3.5073  1.8728  1424     no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 1417) = 36959.9401, p-val < .0001
##
## Test of Moderators (coefficients 1:7):
## QM(df = 7) = 296.1010, p-val < .0001
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## bin.temp<15    -2.1735  0.2641   -8.2295 <.0001   -2.6911   -1.6558 ***
## bin.temp>40    -4.3979  0.3590  -12.2495 <.0001   -5.1015   -3.6942 ***
## bin.temp15-20  -1.3371  0.1863   -7.1772 <.0001   -1.7022   -0.9720 ***
## bin.temp20-25  -0.5413  0.1761   -3.0744  0.0021   -0.8864   -0.1962 **
## bin.temp25-30  -0.2826  0.2064   -1.3690  0.1710   -0.6871    0.1220
## bin.temp30-35  -1.3020  0.1721   -7.5658 <.0001   -1.6393   -0.9647 ***
## bin.temp35-40  -3.0104  0.2449  -12.2907 <.0001   -3.4905   -2.5303 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

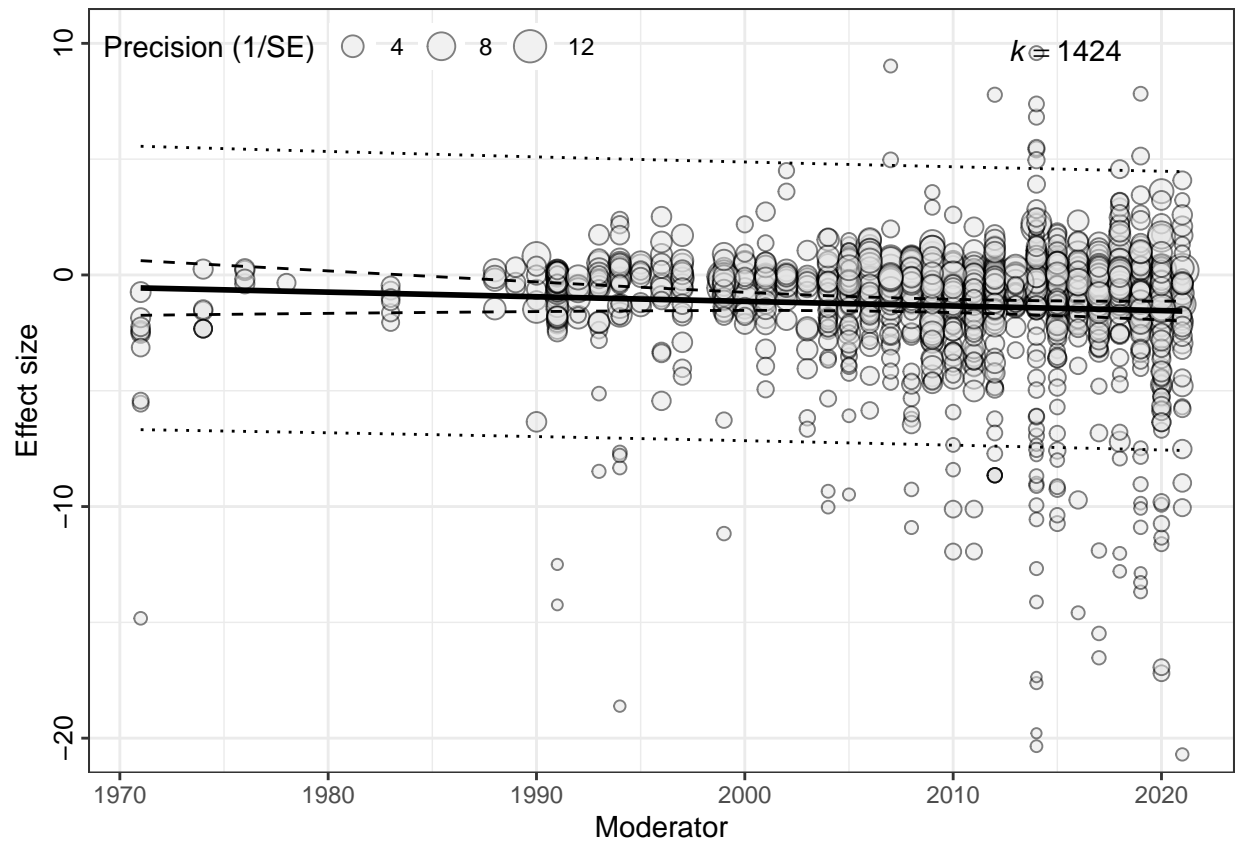
Publication Bias.

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 = 1424; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -3836.8898    7673.7795    7683.7795    7710.0786    7683.8219
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  5.0680  2.2512   340     no      study_code
## sigma^2.2  0.0000  0.0003   468     no  shared_control
## sigma^2.3  4.3155  2.0774  1424     no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 1422) = 39436.4594, p-val < .0001
##
## Test of Moderators (coefficient 2):
## QM(df = 1) = 1.7345, p-val = 0.1878
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt      38.6856  30.3845   1.2732  0.2029  -20.8668   98.2381
## Publication.year -0.0199   0.0151  -1.3170  0.1878   -0.0495    0.0097
##
## ---
## 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%
## -14.17337

print(maxq)

##      97.5%
##  2.346771
```

The summary of the effective sizes is now

```
summary(sdata$es)

##      Min.   1st Qu.   Median     Mean  3rd Qu.     Max.
## -14.1203  -1.8260   -0.6231   -1.3541   0.0000    2.3381
```

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

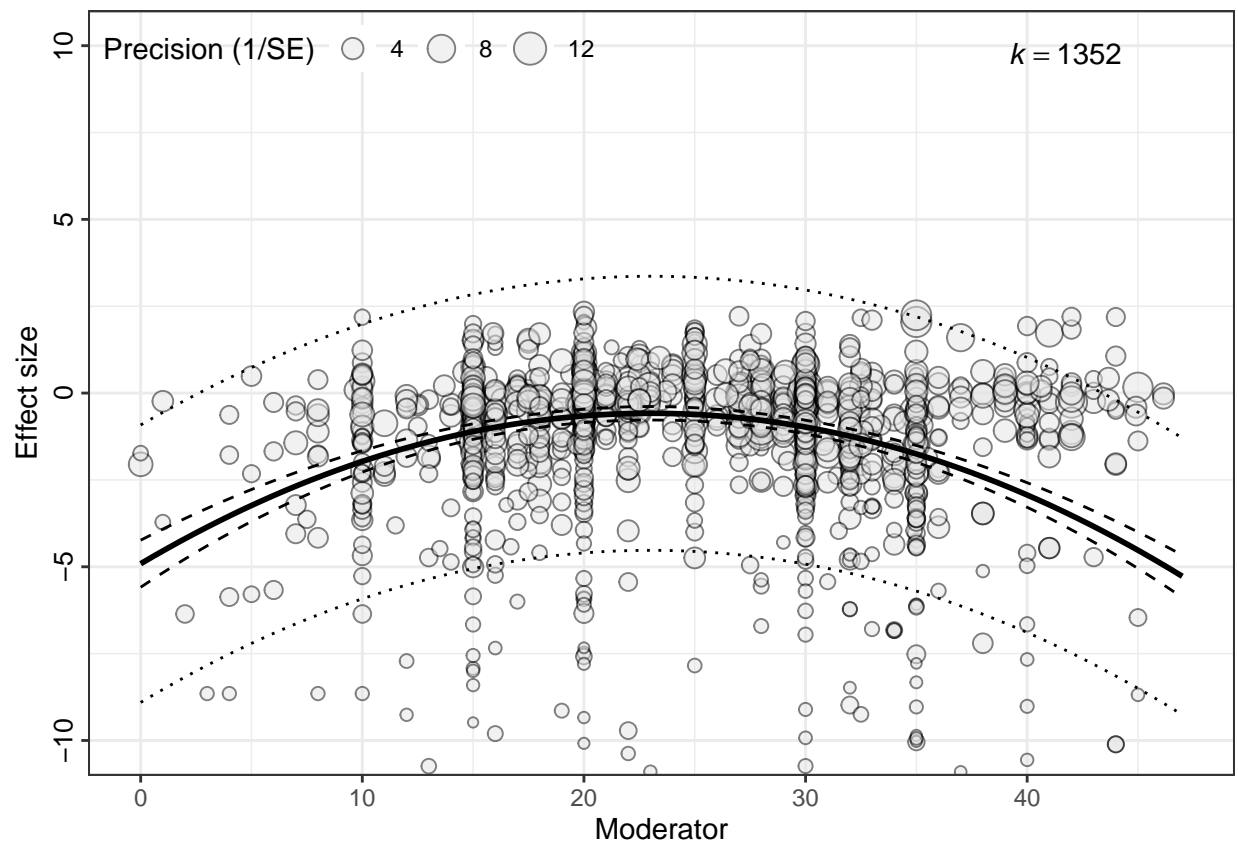
```
meta_sa_treat2 <- rma.mv(es, VCV_shared_sa, mod = ~poly(treattemp,
  degree = 2, raw = TRUE), random = list(~1 | study_code, ~1 |
  shared_control, ~1 | obs), data = sdata, method = "REML")
```

```
summary(meta_sa_treat2)
```

```
##
## Multivariate Meta-Analysis Model (k = 1352; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -2739.7685    5479.5369    5491.5369    5522.7796    5491.5995
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  1.9361  1.3914   334    no      study_code
## sigma^2.2  0.2959  0.5440   458    no  shared_control
## sigma^2.3  1.8094  1.3451  1352    no          obs
##
## Test for Residual Heterogeneity:
## QE(df = 1349) = 29205.7971, p-val < .0001
##
## Test of Moderators (coefficients 2:3):
## QM(df = 2) = 183.0971, p-val < .0001
```

```
##
## Model Results:
##
##               estimate      se      zval      pval      ci.lb      ci.ub
## intrcpt          -4.9115  0.3557  -13.8095 <.0001  -5.6086  -4.2145 ***
## poly(treattemp, degree = 2, raw = TRUE)1    0.3761  0.0303   12.4323 <.0001   0.3168   0.4354 ***
## poly(treattemp, degree = 2, raw = TRUE)2   -0.0082  0.0006  -13.2209 <.0001  -0.0094  -0.0070 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Below is a bubble plot of the fitted quadratic model to the subsetting 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 subsetting data are given below

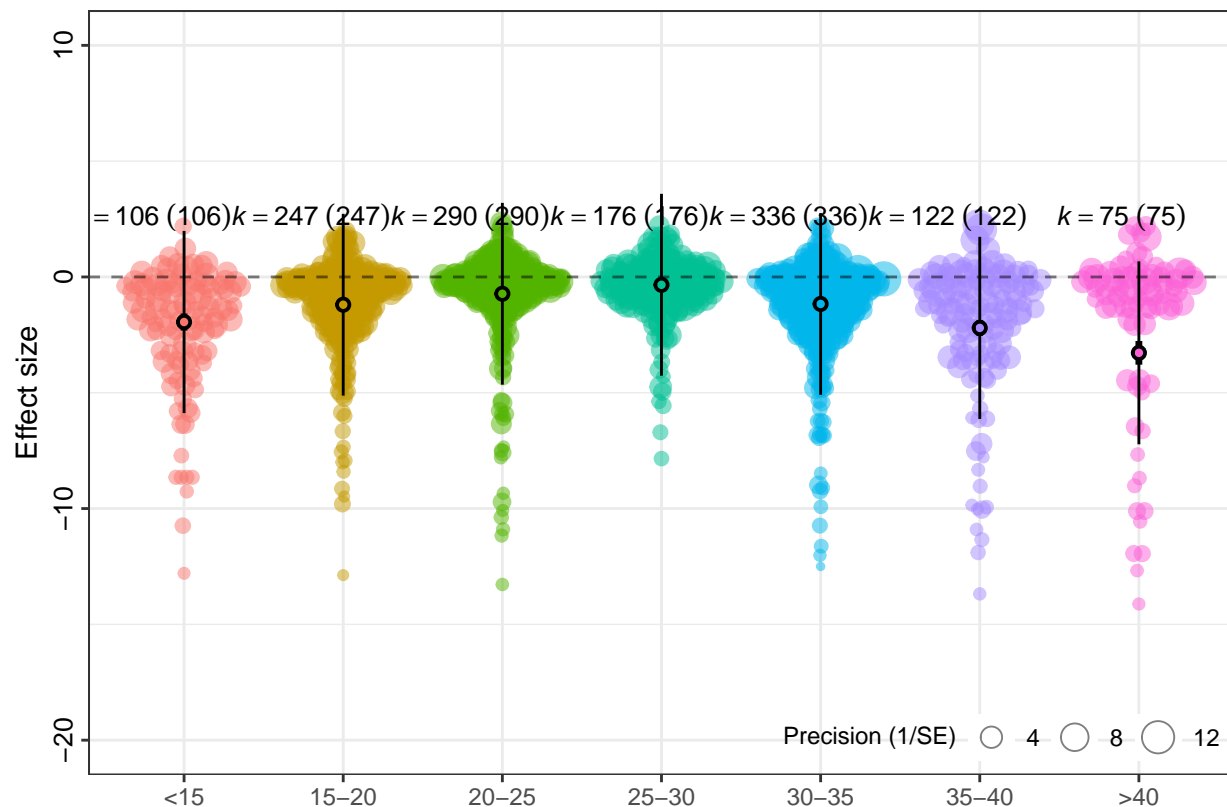
```
table(sdata$bin.temp)
```

```
##
##   <15   >40 15-20 20-25 25-30 30-35 35-40
##   106    75  247   290   176   336   122
```

```
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 = 1352; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -2734.2328    5468.4656    5488.4656    5540.5071    5488.6305
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  1.9053  1.3803   334    no      study_code
## sigma^2.2  0.2400  0.4899   458    no  shared_control
## sigma^2.3  1.8478  1.3593  1352    no      obs
##
## Test for Residual Heterogeneity:
## QE(df = 1345) = 29053.0614, p-val < .0001
##
## Test of Moderators (coefficients 1:7):
## QM(df = 7) = 343.0517, p-val < .0001
##
## Model Results:
##
##      estimate      se      zval      pval      ci.lb      ci.ub
## bin.temp<15    -1.9463  0.1881  -10.3494  <.0001   -2.3149   -1.5777 ***
## bin.temp>40    -3.2768  0.2610  -12.5538  <.0001   -3.7884   -2.7652 ***
## bin.temp15-20  -1.1991  0.1278   -9.3796  <.0001   -1.4496   -0.9485 ***
## bin.temp20-25  -0.7255  0.1217   -5.9628  <.0001   -0.9640   -0.4870 ***
## bin.temp25-30  -0.3384  0.1450   -2.3334  0.0196   -0.6226   -0.0542  *
## bin.temp30-35  -1.1658  0.1169   -9.9724  <.0001   -1.3949   -0.9366 ***
## bin.temp35-40  -2.2001  0.1757  -12.5248  <.0001   -2.5444   -1.8558 ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```



Now we completely remove any study that has an effect size in the highest or lowest 2.5%.

```
summary(meta_sub_bintemp)
```

```
##
## Multivariate Meta-Analysis Model (k = 1254; method: REML)
##
##      logLik      Deviance      AIC      BIC      AICc
## -2373.7443    4747.4887    4767.4887    4818.7736    4767.6667
##
## Variance Components:
##
##      estim      sqrt  nlvls  fixed      factor
## sigma^2.1  1.1726  1.0828   310    no      study_code
## sigma^2.2  0.3382  0.5816   420    no  shared_control
## sigma^2.3  1.4277  1.1948  1254    no              obs
##
## Test for Residual Heterogeneity:
## QE(df = 1247) = 25259.1515, p-val < .0001
##
## Test of Moderators (coefficients 1:7):
## QM(df = 7) = 309.9108, p-val < .0001
##
## Model Results:
```



```
##
##          estimate      se      zval      pval      ci.lb      ci.ub
## bin.temp<15      -1.8603  0.1670  -11.1394  <.0001  -2.1876  -1.5329  ***
## bin.temp>40      -2.2556  0.2503   -9.0123  <.0001  -2.7461  -1.7650  ***
## bin.temp15-20     -1.1425  0.1136  -10.0581  <.0001  -1.3652  -0.9199  ***
## bin.temp20-25     -0.6162  0.1079   -5.7115  <.0001  -0.8277  -0.4048  ***
## bin.temp25-30     -0.3334  0.1287   -2.5906  0.0096  -0.5857  -0.0812   **
## bin.temp30-35     -1.1547  0.1040  -11.0985  <.0001  -1.3587  -0.9508  ***
## bin.temp35-40     -1.7468  0.1609  -10.8597  <.0001  -2.0621  -1.4315  ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```