Meta Analyses Read Me

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The aim of the meta analysis approach is to combine effects from different studies to identify an overall effect. Here, for a given trait, we consider each lab as being a study in which the effect of *Population* has been assessed via a linear mixed-effect model. However, as we are not directly interested in finding overall effects and because *Population* has 9 levels, we perform a subgroup meta analysis that allows to test for differences between populations (each population being considered as a subgroup). In a way, this is conceptually similar to performing a regression analysis to test for the effect of *Population* on a given trait.

The input data for the subgroup meta analysis consists of the estimates and standard errors obtained for *Population* in the trait- and lab-specific linear mixed-effect models. Estimates are used as populations effects, and standard errors of those estimates are used as weights — to give more or less weight to labs depending on sample size and replication level.

This approach can be used to asses differences between populations and generate compound population estimates as input data for downstream analyses. Alternatively, a similar approach can be applied to lines random coefficents extracted from the mixed-effect models (in which *Line* is a random-effect variable) to generate compound line estimates — note that we are not interesting in finding differences between lines here.

1 Population differentiation and estimates

1.1 Input data

Models estimates are located in the LinearModelsPop directory and trait sub directories, in .rds and .csv format (.txt in sub directories). They can be read in as a global list:

```
# read in models estimates for all models as a list
estimates_list <- readRDS("../LinearModelsPop/all_models_pop_estimates_list.rds")
# estimates_list structure
head(lapply(estimates_list, head))
```

```
## $ccrt_lmer
##   Model Predictor Trait    Lab Sex Population Estimate       SE
## 1  lmer       pop  CCRT Vieira   F         AK 1582.022 64.35074
## 2  lmer       pop  CCRT Vieira   F         GI 1526.909 76.79207
## 3  lmer       pop  CCRT Vieira   F         KA 1388.138 63.06706
## 4  lmer       pop  CCRT Vieira   F         MA 1294.829 64.91031
## 5  lmer       pop  CCRT Vieira   F         MU 1532.414 68.01135
## 6  lmer       pop  CCRT Vieira   F         RE 1434.206 67.88454
##
## $csm_lmer
##   Model Predictor Trait      Lab Sex Population Estimate         SE
## 1  lmer       pop   CSM Gonzalez   F         AK 1.323264 0.05405304
## 2  lmer       pop   CSM Gonzalez   F         GI 1.151167 0.05953841
## 3  lmer       pop   CSM Gonzalez   F         KA 1.235156 0.05853235
## 4  lmer       pop   CSM Gonzalez   F         MA 1.236067 0.05420934
```

```
## 5  lmer       pop   CSM Gonzalez   F         MU 1.287623 0.05451414
## 6  lmer       pop   CSM Gonzalez   F         RE 1.213070 0.05710415
##
## $dt_lmer
##   Model Predictor Trait     Lab Sex Population Estimate       SE
## 1  lmer       pop  DT_P Schmidt  NA         AK 127.5020 2.866844
## 2  lmer       pop  DT_P Schmidt  NA         GI 140.4224 3.742029
## 3  lmer       pop  DT_P Schmidt  NA         KA 127.2923 2.882768
## 4  lmer       pop  DT_P Schmidt  NA         MA 132.0037 2.956083
## 5  lmer       pop  DT_P Schmidt  NA         MU 129.7299 2.864570
## 6  lmer       pop  DT_P Schmidt  NA         RE 135.2698 3.346794
##
## $dia_lmer
##   Model Predictor Trait      Lab Sex Population  Estimate         SE
## 1  lmer       pop   Dia Bergland   F         AK 0.8327224 0.07492676
## 2  lmer       pop   Dia Bergland   F         GI 0.8478586 0.08018527
## 3  lmer       pop   Dia Bergland   F         KA 0.9141726 0.06746287
## 4  lmer       pop   Dia Bergland   F         MA 1.0239298 0.07159688
## 5  lmer       pop   Dia Bergland   F         MU 1.0232623 0.07070617
## 6  lmer       pop   Dia Bergland   F         RE 0.8660238 0.08286173
##
## $dw_lmer
##   Model Predictor Trait     Lab Sex Population  Estimate         SE
## 1  lmer       pop    DW Colinet   F         AK 0.4687296 0.01185768
## 2  lmer       pop    DW Colinet   F         GI 0.4799014 0.01310426
## 3  lmer       pop    DW Colinet   F         KA 0.4988845 0.01220288
## 4  lmer       pop    DW Colinet   F         MA 0.5020231 0.01217929
## 5  lmer       pop    DW Colinet   F         MU 0.4844963 0.01185768
## 6  lmer       pop    DW Colinet   F         RE 0.5151915 0.01310339
##
## $fec_lmer
##   Model Predictor Trait      Lab Sex Population  Estimate        SE
## 1  lmer       pop   Fec Billeter   F         AK  97.06708  9.154799
## 2  lmer       pop   Fec Billeter   F         GI  74.19339 10.464893
## 3  lmer       pop   Fec Billeter   F         KA 109.97036  9.128496
## 4  lmer       pop   Fec Billeter   F         MA  99.11960  9.867985
## 5  lmer       pop   Fec Billeter   F         MU  93.84245  9.547513
## 6  lmer       pop   Fec Billeter   F         RE  67.85381 10.896592
```

Alternatively models estimates can be read in as tables for all traits or specific traits only:

```
# read in models estimates for all models as a table
estimates <- readRDS("../LinearModelsPop/all_models_pop_estimates.rds")
# read in models estimates for a specific trait, Viability, as a table
estimates_via <- readRDS("../LinearModelsPop/Viability/Via_lmers_pop_model_estimates.rds")
```

1.2 Meta analyses

We run meta analyses trait- and sex-wise using a random-effect model since we assume that effects measured in each lab do not only deviate because of sampling error alone but also because of other sources of variance — such as lab effect. Model estimates input format is slighty transformed using the makeEffects function before running the analysis.

```
# packages and function
library(meta)
```

```
library(metafor)
source("../Code/functions.R")
```

```
# meta analysis
meta_via <- metagen(data = makeEffects(estimates_list$via_lmer),
                    TE = Y,
                    seTE = SE,
                    studlab = Study,
                    fixed = FALSE,
                    random = TRUE,
                    method.tau = "REML")
```

```
# subgroup meta analysis
meta_via_sub <- update.meta(meta_via, subgroup = Population, tau.common = FALSE)
```

As discussed in early September 2022, partial data (incomple data sets) from Posnien's lab have been removed prior to running Wing Area and Thorax Length analyses.

Importantly meta analyses have been run for all the traits, including those that have been measured in single labs (such as Locomotor Activity and Egg-to-pupa Development Time) and for which there is no data to combine. Obviously, results from these analyses are meaningless but it allows us to keep those traits in the loop and to streamline the generation of compound estimates — that will be equal to linear model estimates in the case of the aforementioned traits. The same applies to Thorax Length males, a trait for which some populations have been measured only in one lab.

1.3 Meta analysis results

All meta analyses related results, compound estimates and graphics are saved in the MetaAnalyses directory and traits sub directories. Below is the structure of a typical trait sub directory:

- _pop_meta.rds: subgroup meta analysis output
- _pop_meta_summary.txt: summary of subgroup meta analysis output
- _pop_meta_compound_estimates.rds (and .txt): population compound estimates
- _pop_meta_summary_effect.pdf (and .png): plot of population summary effects

1.3.1 Model output and results

```
# meta results
readRDS("../MetaAnalyses/Viability/Via_NA_lmers_pop_meta.rds")
```

```
## Number of studies combined: k = 48
##
##                                        95%-CI     z p-value
## Random effects model 0.9550 [0.9300; 0.9799] 75.03       0
##
## Quantifying heterogeneity:
##  tau^2 = 0.0062 [0.0038; 0.0107]; tau = 0.0784 [0.0618; 0.1037]
##  I^2 = 82.2% [77.1%; 86.2%]; H = 2.37 [2.09; 2.69]
##
## Test of heterogeneity:
##       Q d.f.  p-value
##  264.43   47 < 0.0001
##
## Results for subgroups (random effects model):
##                    k                 95%-CI   tau^2    tau     Q   I^2
## Population = YE   5 0.8126 [0.7814; 0.8438]       0      0  2.62  0.0%
```

```
## Population = RE   6 0.9314 [0.9019; 0.9610]       0      0  0.73  0.0%
## Population = GI   5 0.8954 [0.8594; 0.9314] <0.0001 0.0002  6.03 33.6%
## Population = MU   6 0.9886 [0.9400; 1.0371]  0.0023 0.0484 15.49 67.7%
## Population = MA   5 0.9519 [0.8850; 1.0187]  0.0043 0.0653 16.69 76.0%
## Population = UM   5 1.0009 [0.9256; 1.0762]  0.0056 0.0746 18.53 78.4%
## Population = KA   5 1.0330 [0.9799; 1.0861]  0.0022 0.0472 10.25 61.0%
## Population = VA   5 0.9429 [0.8723; 1.0136]  0.0050 0.0704 18.28 78.1%
## Population = AK   6 1.0313 [0.9849; 1.0777]  0.0020 0.0452 13.58 63.2%
##
## Test for subgroup differences (random effects model):
##                        Q d.f.  p-value
## Between groups   100.09    8 < 0.0001
##
## Details on meta-analytical method:
## - Inverse variance method
## - Restricted maximum-likelihood estimator for tau^2
## - Q-profile method for confidence interval of tau^2 and tau
```

To investigate differences between populations one can use the Q value shown in the "Test for subgroup differences (random effects model)" part of the model output. In short, this statistic is a measure of heterogeneity between the different subgroups. Under the null hypothesis of no differences between subgroups Q follows a central χ^2 distribution with degrees of freedom equal to n subgroups - 1, so we can report a p value for any observed value of Q. In the case of Viability, $Q = 100.09$ and is statistically significant ($p < 0.0001$), meaning that populations are indeed different from each other.

1.3.2 Compound population estimates

Compound population estimates (population summary effects) and their 95% confidence intervals can be retrieved from meta analyses outputs. Compound estimates are saved as .rds and .txt files for easier browsing. Below is an example for Viability:

```
# read in population compound estimates
comp_pop_via <- readRDS("../MetaAnalyses/Viability/Via_NA_lmers_pop_meta_compound_estimates.rds")
print(select(comp_pop_via, -c(Models, Sex, SE, N_lab_av))) # for clarity
```

```
##   Trait Population  Estimate     LLEst     ULEst        Q            P N_lab
## 1   Via         YE 0.8125780 0.7813953 0.8437606 100.0945 4.083404e-18     5
## 2   Via         RE 0.9314387 0.9018622 0.9610153 100.0945 4.083404e-18     6
## 3   Via         GI 0.8953657 0.8593534 0.9313780 100.0945 4.083404e-18     5
## 4   Via         MU 0.9885519 0.9400152 1.0370886 100.0945 4.083404e-18     6
## 5   Via         MA 0.9518613 0.8850298 1.0186928 100.0945 4.083404e-18     5
## 6   Via         UM 1.0009199 0.9255974 1.0762424 100.0945 4.083404e-18     5
## 7   Via         KA 1.0329804 0.9798800 1.0860809 100.0945 4.083404e-18     5
## 8   Via         VA 0.9429267 0.8722642 1.0135892 100.0945 4.083404e-18     5
## 9   Via         AK 1.0312744 0.9848986 1.0776502 100.0945 4.083404e-18     6
```

Results can be represented with a simplified forest plot where populations summary effects (compound estimates) and populations are represented on x and y axis, respectively (Figure 1). These plots have been produced for each trait and sex (when applicable) and can be found in the traits sub directories as .pdf and .png files.

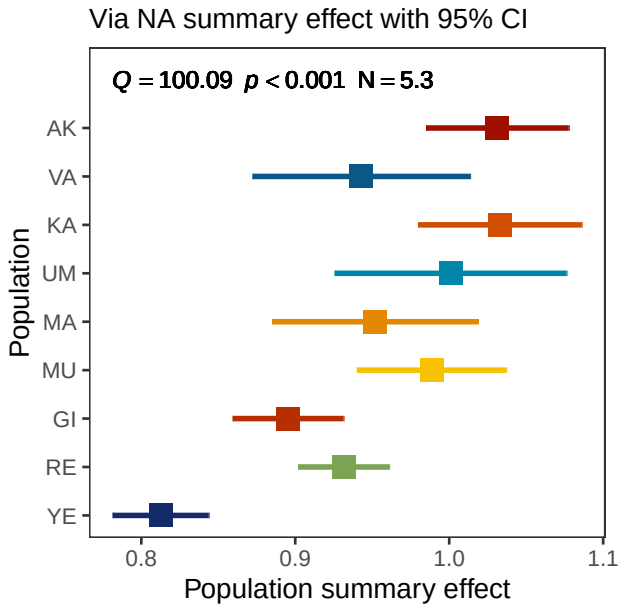

Figure 1: Subgroup meta analysis for Viability. N indicates the average number of labs that have phenotyped the different populations.

1.3.3 Compiled data

Compiled population compound estimates, meta analyses statistics and composite figures for all traits are available in the MetaAnalyses directory.

Meta analyses main statistics. All meta analyses main statistics have been compiled in a single table. *P* values were corrected for multiple testing using Bonferroni and Benjamini Hochberg procedures (number of tests = 26 — corresponds to the number of "relevant" meta analyses that have been performed, see above). As mentioned earlier, statistics for Locomotor Activity, Egg-to-pupa Development Time and Thorax Length in males should not be considered and have been filtered out from this table:

```
## [1] "all_models_pop_meta_pvalues.csv" "all_models_pop_meta_pvalues.rds"
```

```
# meta p values
readRDS("../MetaAnalyses/all_models_pop_meta_pvalues.rds") %>% head()
```

```
##   Models Trait Sex         Q         P Min_lab Max_lab P_bonf      P_bh
## 1  lmers  CCRT   F  8.684978 0.3695636       2       2      1 0.6405770
## 2  lmers  CCRT   M 12.169043 0.1438195       2       2      1 0.3739307
## 3  lmers   CSM   F  1.051165 0.9979040       3       3      1 0.9979040
## 4  lmers   CSM   M  4.720664 0.7869719       3       3      1 0.9743462
## 5  lmers  DT_A   F  7.607906 0.4726764       5       6      1 0.7229169
## 6  lmers  DT_A   M  8.745727 0.3641982       5       6      1 0.6405770
```

Meta analyses main statistics plot. (Figure 2):

```
## [1] "all_models_pop_meta_pvalues.pdf"
```

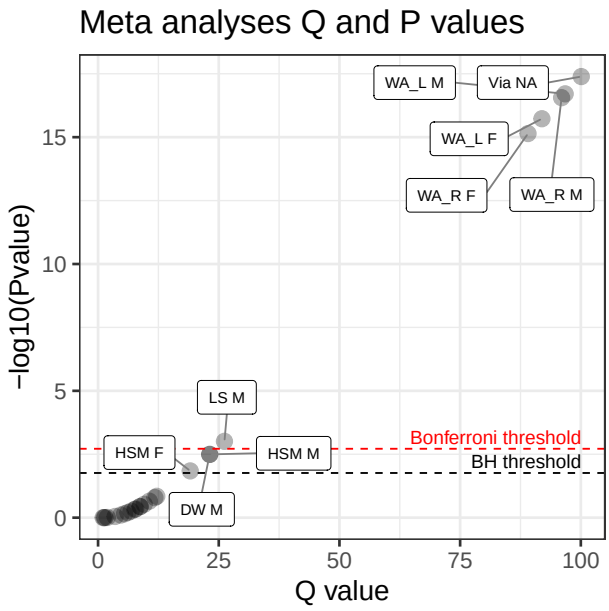

Figure 2: All meta analyses Q and p values.

Compound estimates. Compiled for all traits as list or table:

```
## [1] "all_models_pop_meta_compound_estimates_list.rds"
## [2] "all_models_pop_meta_compound_estimates.csv"
## [3] "all_models_pop_meta_compound_estimates.rds"
```

```
# population compoud estimates as list
comp_pop_list <- readRDS("../MetaAnalyses/all_models_pop_meta_compound_estimates_list.rds")
lapply(comp_pop_list, function(x) select(x, -c(Models, SE, N_lab_av))) %>% head()
```

```
## $CCRT_F_lmers_pop_meta_compound_estimates
##   Trait Sex Population Estimate    LLEst    ULEst        Q         P N_lab
## 1  CCRT   F         YE 1686.687 1276.713 2096.660 8.684978 0.3695636     2
## 2  CCRT   F         RE 1534.213 1319.867 1748.560 8.684978 0.3695636     2
## 3  CCRT   F         GI 1516.612 1397.093 1636.132 8.684978 0.3695636     2
## 4  CCRT   F         MU 1646.321 1411.554 1881.087 8.684978 0.3695636     2
## 5  CCRT   F         MA 1541.103 1052.333 2029.872 8.684978 0.3695636     2
## 6  CCRT   F         UM 1786.288 1622.238 1950.338 8.684978 0.3695636     2
## 7  CCRT   F         KA 1515.422 1254.197 1776.647 8.684978 0.3695636     2
## 8  CCRT   F         VA 1556.032 1243.886 1868.179 8.684978 0.3695636     2
## 9  CCRT   F         AK 1701.556 1455.533 1947.580 8.684978 0.3695636     2
##
## $CCRT_M_lmers_pop_meta_compound_estimates
##   Trait Sex Population Estimate    LLEst    ULEst        Q         P N_lab
## 1  CCRT   M         YE 1729.246 1558.606 1899.886 12.16904 0.1438195     2
## 2  CCRT   M         RE 1542.950 1437.879 1648.021 12.16904 0.1438195     2
## 3  CCRT   M         GI 1752.887 1556.901 1948.872 12.16904 0.1438195     2
## 4  CCRT   M         MU 1690.640 1595.557 1785.724 12.16904 0.1438195     2
## 5  CCRT   M         MA 1479.440 1176.635 1782.246 12.16904 0.1438195     2
## 6  CCRT   M         UM 1610.294 1511.261 1709.327 12.16904 0.1438195     2
## 7  CCRT   M         KA 1598.621 1289.433 1907.809 12.16904 0.1438195     2
## 8  CCRT   M         VA 1526.679 1431.565 1621.793 12.16904 0.1438195     2
```

```
## 9  CCRT   M         AK 1666.717 1451.398 1882.035 12.16904 0.1438195     2
##
## $CSM_F_lmers_pop_meta_compound_estimates
##   Trait Sex Population Estimate     LLEst    ULEst        Q        P N_lab
## 1   CSM   F         YE 1.155249 0.8953922 1.415107 1.051165 0.997904     3
## 2   CSM   F         RE 1.112459 0.8547746 1.370143 1.051165 0.997904     3
## 3   CSM   F         GI 1.112156 0.9147955 1.309516 1.051165 0.997904     3
## 4   CSM   F         MU 1.155516 0.8849492 1.426083 1.051165 0.997904     3
## 5   CSM   F         MA 1.117443 0.8297335 1.405152 1.051165 0.997904     3
## 6   CSM   F         UM 1.031687 0.7821792 1.281194 1.051165 0.997904     3
## 7   CSM   F         KA 1.131730 0.8100121 1.453447 1.051165 0.997904     3
## 8   CSM   F         VA 1.161708 0.8518418 1.471574 1.051165 0.997904     3
## 9   CSM   F         AK 1.193219 0.9625454 1.423892 1.051165 0.997904     3
##
## $CSM_M_lmers_pop_meta_compound_estimates
##   Trait Sex Population  Estimate     LLEst    ULEst        Q         P N_lab
## 1   CSM   M         YE 1.1867956 0.9915225 1.382069 4.720664 0.7869719     3
## 2   CSM   M         RE 1.0080916 0.8588830 1.157300 4.720664 0.7869719     3
## 3   CSM   M         GI 1.0431651 0.9349974 1.151333 4.720664 0.7869719     3
## 4   CSM   M         MU 1.0725449 0.8275978 1.317492 4.720664 0.7869719     3
## 5   CSM   M         MA 1.0075638 0.8929595 1.122168 4.720664 0.7869719     3
## 6   CSM   M         UM 0.9466504 0.8097001 1.083601 4.720664 0.7869719     3
## 7   CSM   M         KA 1.0541057 0.9523560 1.155855 4.720664 0.7869719     3
## 8   CSM   M         VA 1.0186589 0.8371505 1.200167 4.720664 0.7869719     3
## 9   CSM   M         AK 1.0007472 0.8707303 1.130764 4.720664 0.7869719     3
##
## $DT_A_F_lmers_pop_meta_compound_estimates
##   Trait Sex Population Estimate    LLEst    ULEst        Q         P N_lab
## 1  DT_A   F         YE 226.6044 218.6626 234.5462 7.607906 0.4726764     5
## 2  DT_A   F         RE 249.7712 220.3431 279.1992 7.607906 0.4726764     6
## 3  DT_A   F         GI 231.9436 224.5747 239.3125 7.607906 0.4726764     5
## 4  DT_A   F         MU 240.0011 213.6781 266.3241 7.607906 0.4726764     6
## 5  DT_A   F         MA 229.6200 221.4252 237.8149 7.607906 0.4726764     5
## 6  DT_A   F         UM 230.7389 220.0798 241.3980 7.607906 0.4726764     5
## 7  DT_A   F         KA 225.7441 221.6158 229.8725 7.607906 0.4726764     5
## 8  DT_A   F         VA 234.5845 223.7638 245.4052 7.607906 0.4726764     5
## 9  DT_A   F         AK 240.0252 211.9969 268.0535 7.607906 0.4726764     6
##
## $DT_A_M_lmers_pop_meta_compound_estimates
##   Trait Sex Population Estimate    LLEst    ULEst        Q         P N_lab
## 1  DT_A   M         YE 231.3565 222.3777 240.3352 8.745727 0.3641982     5
## 2  DT_A   M         RE 253.0096 223.6041 282.4150 8.745727 0.3641982     6
## 3  DT_A   M         GI 239.4041 231.1339 247.6744 8.745727 0.3641982     5
## 4  DT_A   M         MU 245.5187 218.6853 272.3521 8.745727 0.3641982     6
## 5  DT_A   M         MA 234.0428 225.1518 242.9337 8.745727 0.3641982     5
## 6  DT_A   M         UM 235.4982 224.7393 246.2572 8.745727 0.3641982     5
## 7  DT_A   M         KA 229.4707 224.1718 234.7697 8.745727 0.3641982     5
## 8  DT_A   M         VA 239.7320 227.7507 251.7133 8.745727 0.3641982     5
## 9  DT_A   M         AK 246.2465 217.5973 274.8957 8.745727 0.3641982     6
```

Composite figures of all meta analyses results. (Figure 3):

```
## [1] "all_models_pop_meta_summary_effect.pdf"
## [2] "all_models_pop_meta_summary_effect.png"
```

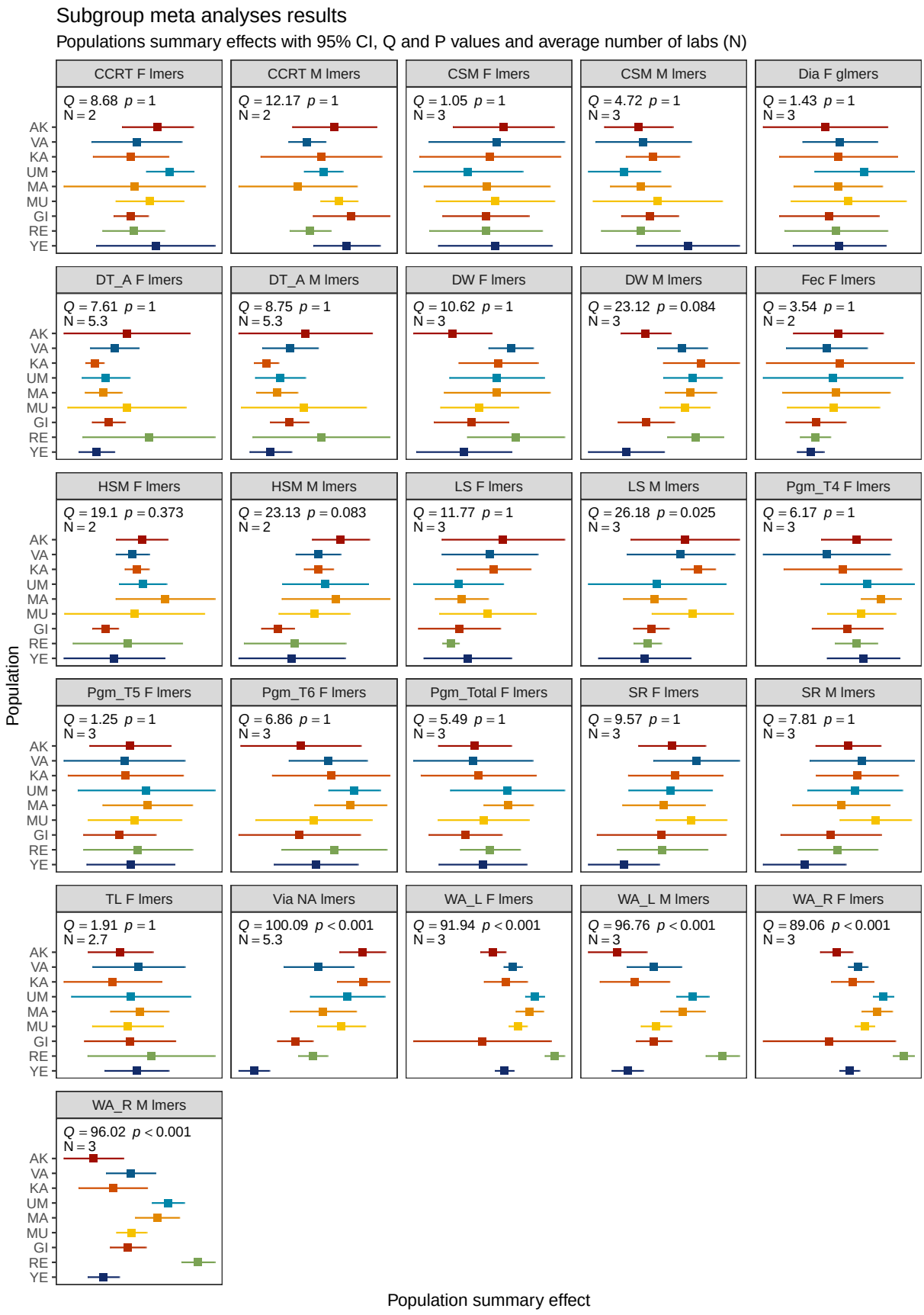

Figure 3: All meta analyses results.

2 Line estimates

2.1 Input data

2.2 Meta analysis

2.3 Meta analysis results

2.3.1 Model output and results

2.3.2 Compound lines estimates