Overall Results

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Meta-analysis

Calculating effect sizes

Here, we calculated our effect sizes (log response ratio lnRR) for our complete data set (all traits).

Meta-analysis overall results (lnRR)

1. Calculating effect sizes (Done)

We calculated our effect sizes (log response ratio lnRR) for our complete data set (all traits).

2. Deciding random effects (Done)

We used AIC values to decide which random effects to use. Combining "Trait", "ES_ID",Paper_ID" and "Cohort_ID" yielded the lowest AIC values.

3. Running meta-analysis (overall, with and without moderators)

I conducted meta-analysis, first on the complete dataset, with and without moderators.

```
#ALL DATA

All_Traits_Analysis_0mods <- rma.mv(yi, vi, random = list(~1|Trait, ~1|Paper_ID,~1|Cohort_ID,~1|ES_ID),

summary(All_Traits_Analysis_0mods)
```

```
##
## Multivariate Meta-Analysis Model (k = 341; method: REML)
##
##   logLik  Deviance       AIC       BIC      AICc
## -66.3761  132.7521  142.7521  161.8968  142.9318
##
## Variance Components:
##
##              estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0155  0.1246      8     no      Trait
## sigma^2.2  0.0859  0.2931     25     no    Paper_ID
## sigma^2.3  0.0080  0.0892     75     no   Cohort_ID
## sigma^2.4  0.0301  0.1736    341     no      ES_ID
##
## Test for Heterogeneity:
## Q(df = 340) = 7077.4171, p-val < .0001
##
## Model Results:
```

```
## 
## estimate       se     zval     pval    ci.lb    ci.ub
##    0.2131   0.0773   2.7563   0.0058   0.0616   0.3646   **
## 
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_0mods)
```
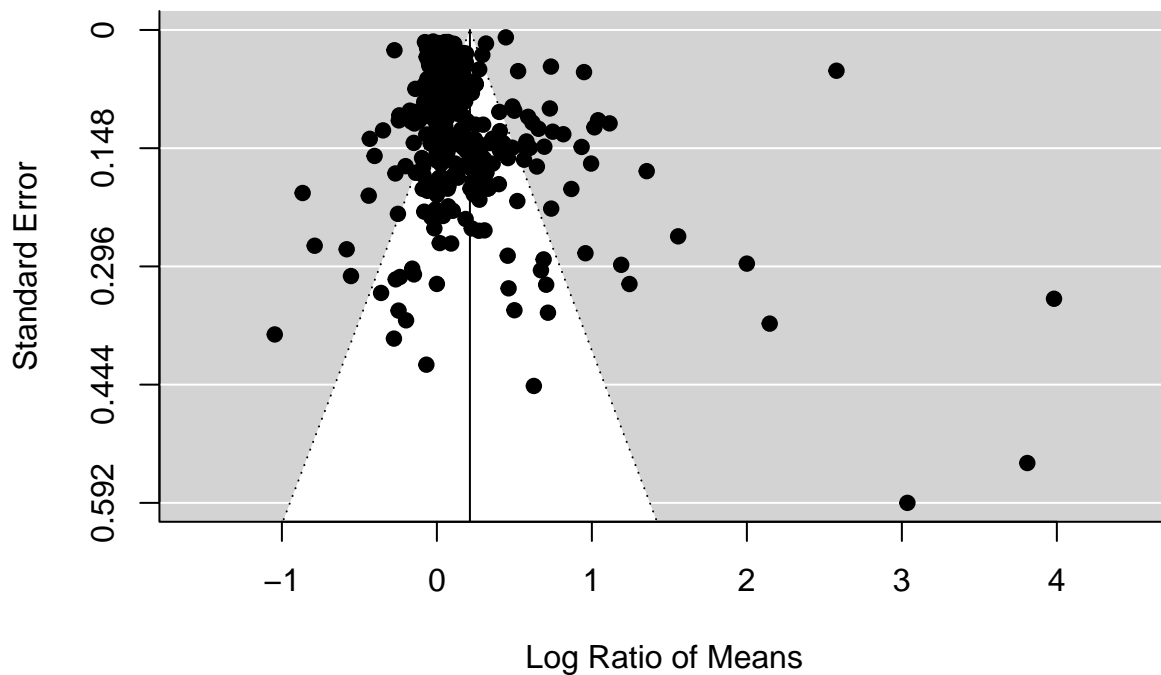


```
W <- diag(1/Effect_Size_All_Traits$vi)
X <- model.matrix(All_Traits_Analysis_0mods)
P <- W - W %*% X %*% solve(t(X) %*% W %*% X) %*% t(X) %*% W
I2_overall <- 100 * sum(All_Traits_Analysis_0mods$sigma2) / (sum(All_Traits_Analysis_0mods$sigma2) + (A
I2_overall
```

```
## [1] 98.28773
```

```
Overall_effect_size <- tibble(
  ID = "Overall",
  lnRR = c(0.2125),
  ci.lb = c(0.0609),
  ci.ub = c(0.3642),
  k = 241
)
```

```
## Warning: `list_len()` is deprecated as of rlang 0.2.0.
## Please use `new_list()` instead.
## This warning is displayed once per session.
```

```
plot_lnRR_overall <- ggplot(Overall_effect_size, aes(x=ID, y=lnRR)) +
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = ID, y = lnRR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "ID", y = "lnRR", subtitle = "k=341") +
  coord_flip()
plot_lnRR_overall
```
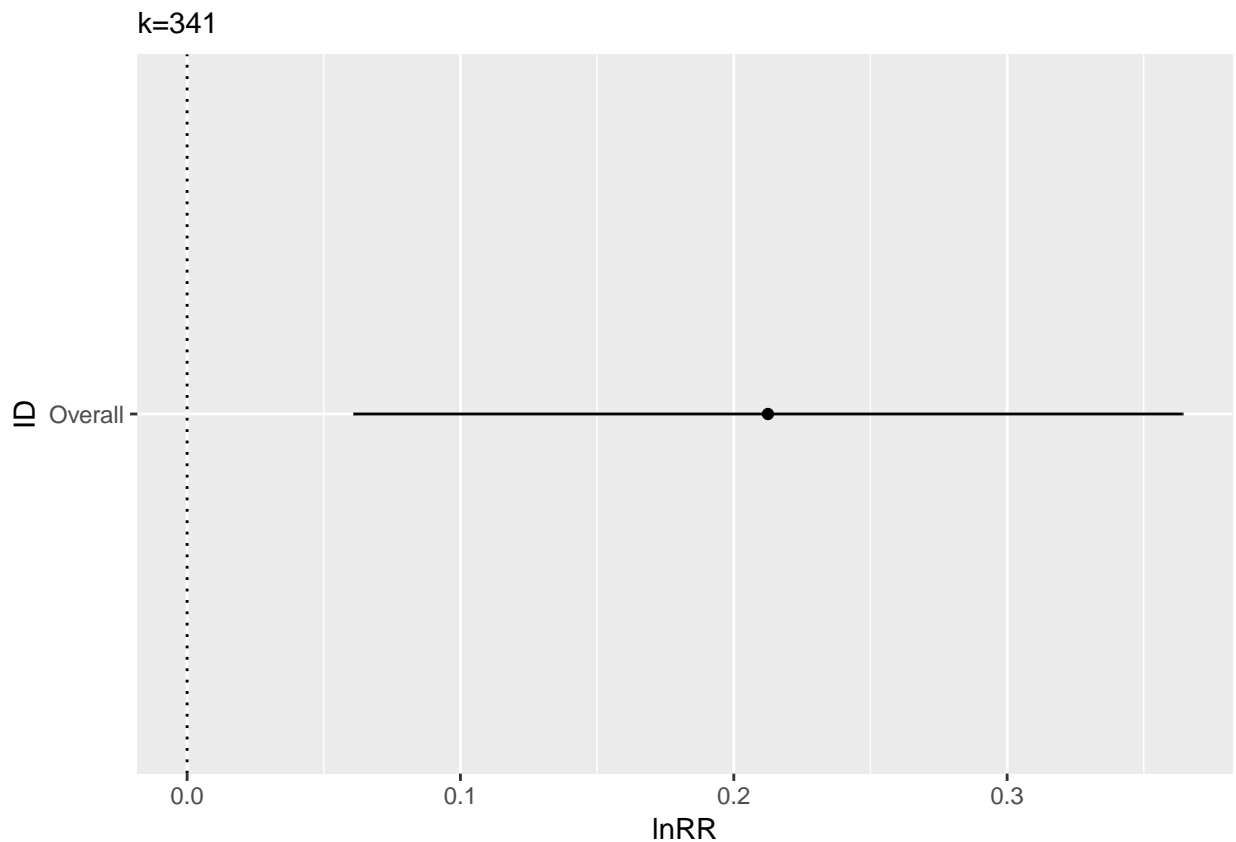

Meta Regression for Traits and Exposure Type

```
### Meta Regression

#Traits meta-regression
All_Traits_Analysis_traits <- rma.mv(yi, vi, mods= ~Trait-1, random = list(~1|Paper_ID,~1|Cohort_ID,~1|

summary(All_Traits_Analysis_traits)
```

```
##
## Multivariate Meta-Analysis Model (k = 341; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -58.7230   117.4459   139.4459   181.3355   140.2684
```

```
## 
## Variance Components:
## 
##             estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0845  0.2908     25     no    Paper_ID
## sigma^2.2  0.0081  0.0902     75     no   Cohort_ID
## sigma^2.3  0.0303  0.1742    341     no       ES_ID
## 
## Test for Residual Heterogeneity:
## QE(df = 333) = 6097.4737, p-val < .0001
## 
## Test of Moderators (coefficient(s) 1:8):
## QM(df = 8) = 84.3701, p-val < .0001
## 
## Model Results:
## 
##                     estimate      se    zval    pval    ci.lb   ci.ub
## TraitAdiposity        0.4111  0.0706  5.8223  <.0001   0.2727  0.5494  ***
## TraitBody_Weight      0.1074  0.0628  1.7103  0.0872  -0.0157  0.2305   .
## TraitGlucose_FBG      0.0412  0.0864  0.4766  0.6337  -0.1282  0.2105
## TraitGlucose_TT       0.1342  0.0732  1.8327  0.0668  -0.0093  0.2777   .
## TraitInsulin_FI       0.2525  0.0817  3.0911  0.0020   0.0924  0.4126  **
## TraitInsulin_TT       0.1371  0.0825  1.6618  0.0966  -0.0246  0.2988   .
## TraitLeptin           0.4078  0.0963  4.2350  <.0001   0.2190  0.5965  ***
## TraitTriglycerides    0.2457  0.0748  3.2850  0.0010   0.0991  0.3923  **
## 
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
funnel(All_Traits_Analysis_traits,yaxis="seinv")
```
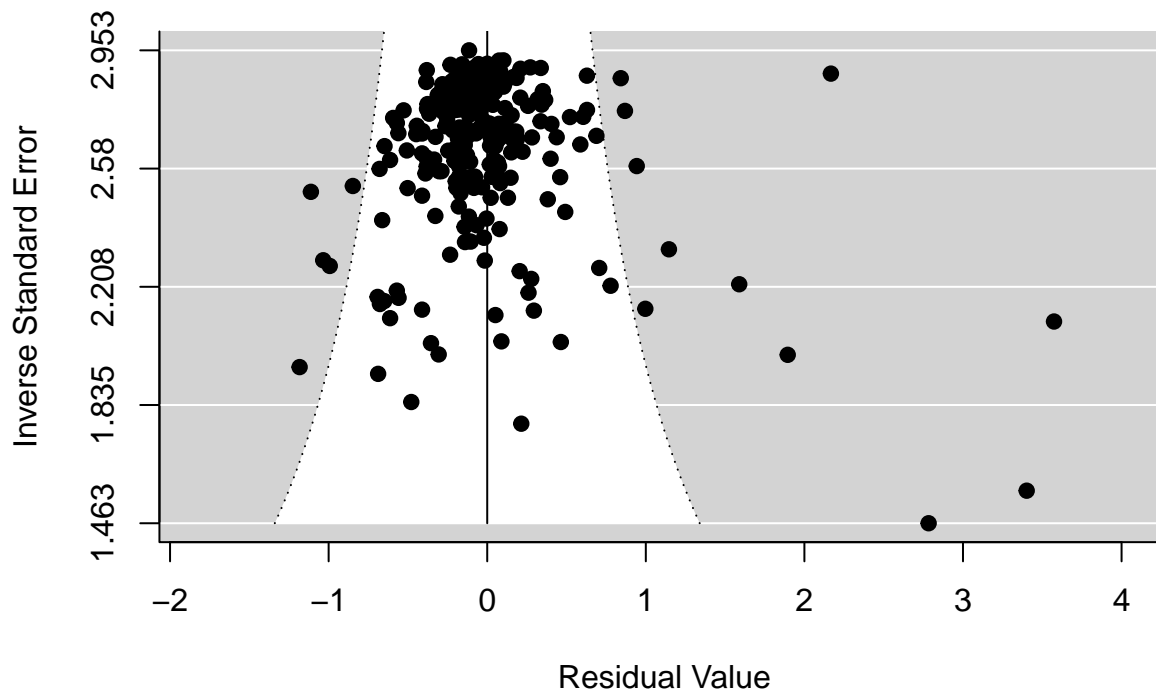
```
k_traits <- Effect_Size_All_Traits %>% group_by(Trait) %>% count()
```

```
## Warning: The `printer` argument is deprecated as of rlang 0.3.0.
## This warning is displayed once per session.
```

```
k_traits
```

```
## # A tibble: 8 x 2
## # Groups:   Trait [8]
##    Trait             n
##    <fct>         <int>
## 1 Adiposity        65
## 2 Body_Weight     146
## 3 Glucose_FBG      12
## 4 Glucose_TT       28
## 5 Insulin_FI       26
## 6 Insulin_TT       19
## 7 Leptin           12
## 8 Triglycerides    33
```

```
Traits_overall_lnRR <- tibble(
  Trait = c("Adiposity", "Body Weight","Glucose FBG", "Glucose TT", "Insulin FI","Insulin TT", "Leptin"
  lnRR = c(0.4111,0.1076,0.0404,0.1349,0.2527,0.1307,0.4073,0.2457),
  ci.lb = c(0.2730,-0.0153,-0.1286,-0.0084,0.0931,-0.0374,0.2189,0.0994),
```

```
    ci.ub = c(0.5492,0.2304,0.2094,0.2782,0.4123,0.2988,0.5957,0.3920),
    k = c(k_traits$n[1],k_traits$n[2],k_traits$n[3],k_traits$n[4],k_traits$n[5],k_traits$n[6],k_traits$n[7
)
Traits_overall_lnRR
```

```
## # A tibble: 8 x 5
##   Trait         lnRR   ci.lb ci.ub    k
##   <chr>         <dbl>  <dbl> <dbl> <int>
## 1 Adiposity     0.411  0.273 0.549    65
## 2 Body Weight   0.108 -0.0153 0.230   146
## 3 Glucose FBG   0.0404 -0.129 0.209    12
## 4 Glucose TT    0.135 -0.0084 0.278    28
## 5 Insulin FI    0.253  0.0931 0.412    26
## 6 Insulin TT    0.131 -0.0374 0.299    19
## 7 Leptin        0.407  0.219 0.596    12
## 8 Triglycerides 0.246  0.0994 0.392    33
```
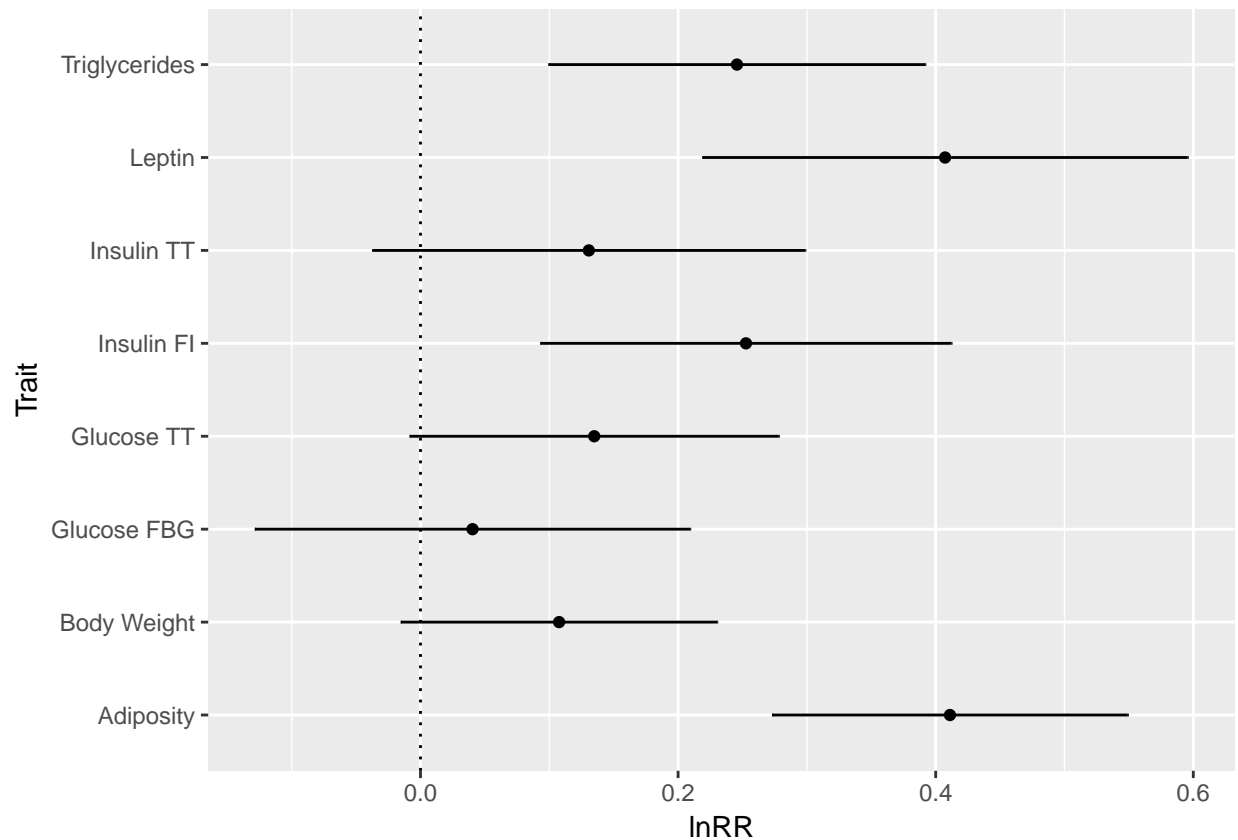
```
plot_lnRR_overall_traits <- ggplot(Traits_overall_lnRR, aes(x=Trait, y=lnRR)) +
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = Trait, y = lnRR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "Trait", y = "lnRR") +
  coord_flip()
plot_lnRR_overall_traits
```

```
#Exposure type meta-regression
All_Traits_Analysis_Exp <- rma.mv(yi, vi, mods= ~Exposure_Type-1, random = list(~1|Paper_ID,~1|Cohort_I

summary(All_Traits_Analysis_Exp)
```

```
##
## Multivariate Meta-Analysis Model (k = 341; method: REML)
##
##    logLik  Deviance       AIC       BIC      AICc
## -82.2231  164.4462  174.4462  193.5762  174.6264
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0887  0.2979     25     no    Paper_ID
## sigma^2.2  0.0028  0.0533     75     no   Cohort_ID
## sigma^2.3  0.0417  0.2041    341     no       ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 339) = 6278.3587, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:2):
## QM(df = 2) = 28.6603, p-val < .0001
##
## Model Results:
##
##                                 estimate      se    zval    pval    ci.lb
## Exposure_TypeMultigenerational    0.3137  0.0704  4.4580  <.0001   0.1758
## Exposure_TypeOne off              0.0626  0.0669  0.9363  0.3491  -0.0684
##                                    ci.ub
## Exposure_TypeMultigenerational    0.4515  ***
## Exposure_TypeOne off              0.1937
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_Exp)
```
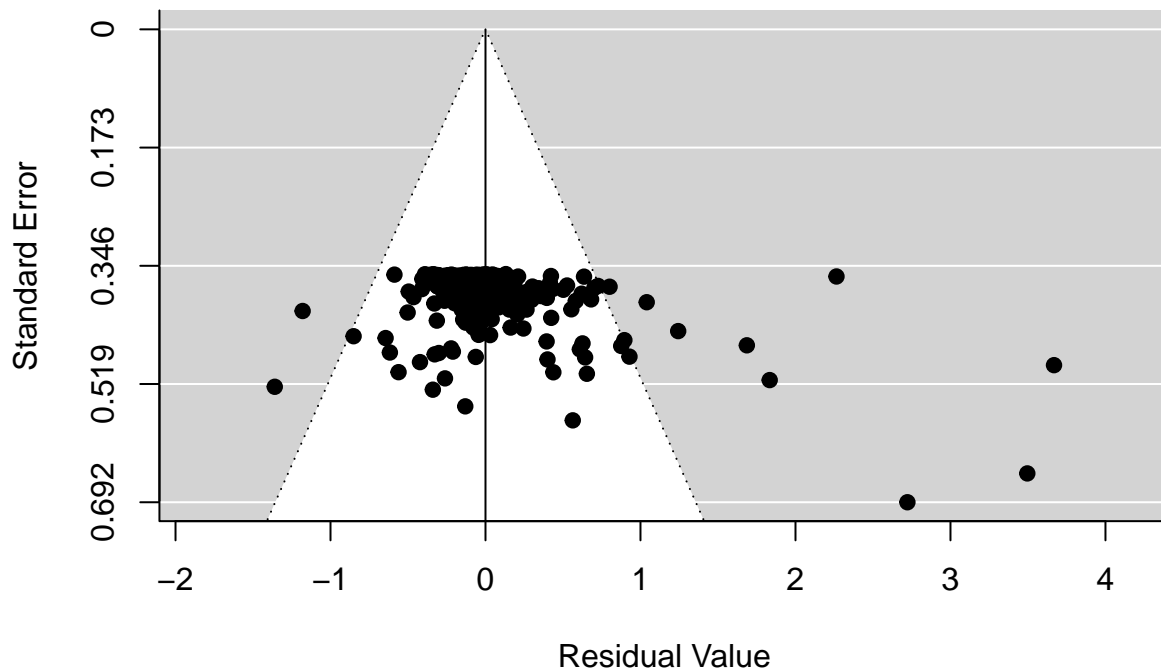
```
k_exp <- Effect_Size_All_Traits %>% group_by(Exposure_Type) %>% count()
k_exp
```

```
## # A tibble: 2 x 2
## # Groups:   Exposure_Type [2]
##   Exposure_Type       n
##   <fct>           <int>
## 1 Multigenerational  118
## 2 One off            223
```

```
Overall_Exp_meta_lnRR <- tibble(
  Exposure_Type = c("Multigenerational", "One off"),
  lnRR = c(0.3121,0.0632),
  ci.lb = c(0.1740,-0.0679),
  ci.ub = c(0.4502,0.1943),
  k = c(k_exp$n[1],k_exp$n[2])
)
Overall_Exp_meta_lnRR
```

```
## # A tibble: 2 x 5
##   Exposure_Type      lnRR   ci.lb ci.ub     k
##   <chr>             <dbl>   <dbl> <dbl> <int>
## 1 Multigenerational 0.312   0.174  0.450   118
## 2 One off           0.0632 -0.0679 0.194   223
```
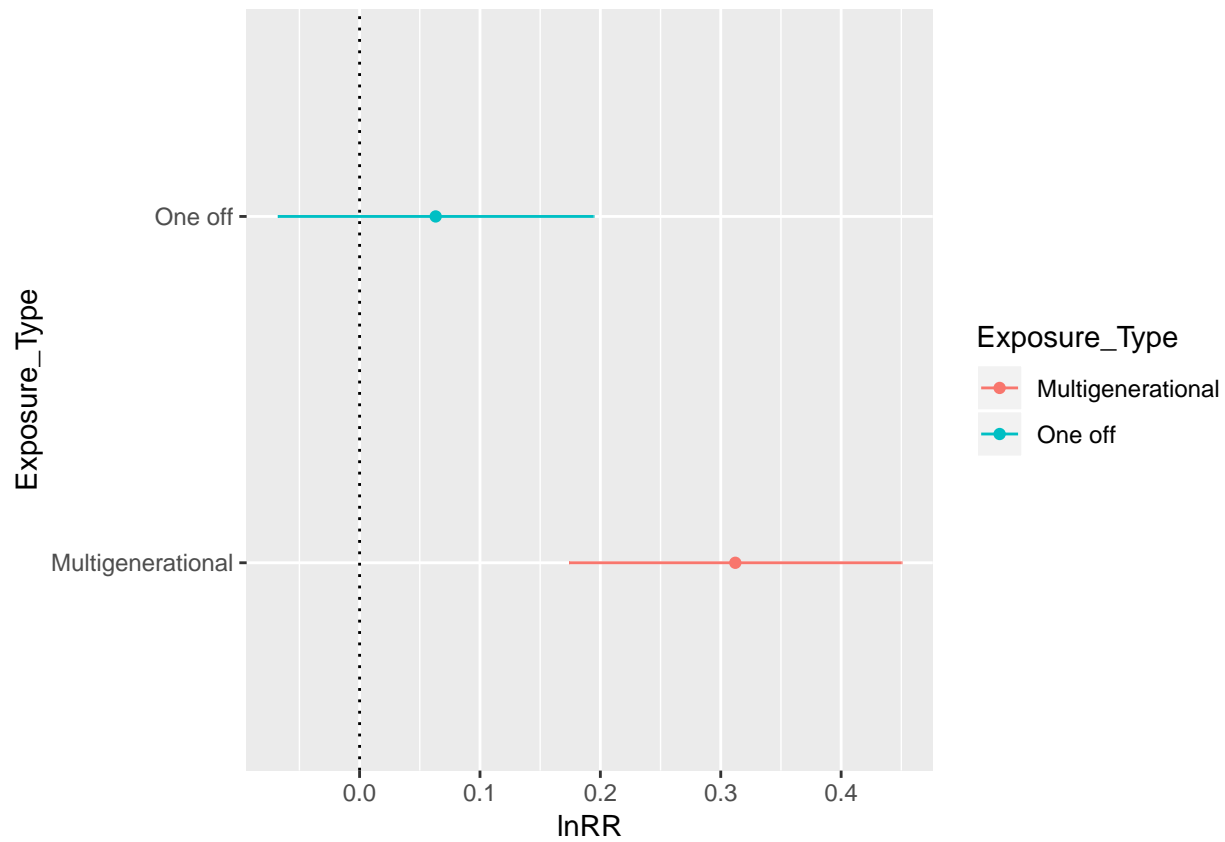
```
plot_lnRR_overall_expmeta <- ggplot(Overall_Exp_meta_lnRR, aes(x=Exposure_Type, y=lnRR, colour=Exposure_
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = Exposure_Type, y = lnRR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "Exposure_Type", y = "lnRR") +
  coord_flip()
plot_lnRR_overall_expmeta
```


Meta-regression of overall dataset for F0 parent and offspring sex

```
All_Data_Analysis_f0 <- rma.mv(yi, vi, mods = ~F0_Parent_Exposed-1, random = list(~1|Trait, ~1|Paper_ID

summary(All_Data_Analysis_f0)
```

```
##
## Multivariate Meta-Analysis Model (k = 341; method: REML)
##
##    logLik   Deviance       AIC        BIC       AICc
## -65.4490   130.8979   144.8979   171.6592   145.2373
##
## Variance Components:
##
##               estim     sqrt   nlvls   fixed      factor
```

9

```
## sigma^2.1  0.0155  0.1245       8      no     Trait
## sigma^2.2  0.0867  0.2945      25      no   Paper_ID
## sigma^2.3  0.0081  0.0898      75      no  Cohort_ID
## sigma^2.4  0.0302  0.1738     341      no      ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 338) = 7056.6821, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:3):
## QM(df = 3) = 8.8141, p-val = 0.0319
##
## Model Results:
##
##                        estimate      se    zval    pval    ci.lb   ci.ub
## F0_Parent_ExposedBoth     0.2760  0.1645  1.6783  0.0933  -0.0463  0.5984
## F0_Parent_ExposedFemale   0.2245  0.0793  2.8322  0.0046   0.0691  0.3799
## F0_Parent_ExposedMale     0.1442  0.1187  1.2149  0.2244  -0.0884  0.3767
##
## F0_Parent_ExposedBoth     .
## F0_Parent_ExposedFemale   **
## F0_Parent_ExposedMale
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
k_All_Data_Analysis_f0 <- Effect_Size_All_Traits %>% group_by(F0_Parent_Exposed) %>% count()
k_All_Data_Analysis_f0
```

```
## # A tibble: 3 x 2
## # Groups:   F0_Parent_Exposed [3]
##   F0_Parent_Exposed     n
##   <fct>             <int>
## 1 Both                  4
## 2 Female              262
## 3 Male                 75
```

```
All_Data_Analysis_sex <- rma.mv(yi, vi, mods = ~Sex-1, random = list(~1|Trait, ~1|Paper_ID,~1|Cohort_ID

summary(All_Data_Analysis_sex)
```

```
##
## Multivariate Meta-Analysis Model (k = 341; method: REML)
##
##   logLik  Deviance      AIC       BIC      AICc
## -64.9763  129.9526  143.9526  170.7139  144.2920
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0151  0.1229      8     no      Trait
## sigma^2.2  0.0994  0.3152     25     no   Paper_ID
## sigma^2.3  0.0079  0.0889     75     no  Cohort_ID
## sigma^2.4  0.0300  0.1733    341     no      ES_ID
```

```
## 
## Test for Residual Heterogeneity:
## QE(df = 338) = 6792.7330, p-val < .0001
## 
## Test of Moderators (coefficient(s) 1:3):
## QM(df = 3) = 9.6342, p-val = 0.0219
## 
## Model Results:
## 
##            estimate      se    zval    pval    ci.lb   ci.ub
## SexBoth      0.3040  0.1628  1.8667  0.0619  -0.0152  0.6231     .
## SexFemale    0.1708  0.0855  1.9973  0.0458   0.0032  0.3385   *
## SexMale      0.2202  0.0852  2.5854  0.0097   0.0533  0.3871  **
## 
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
Overall_effects_not_split_f0_sex <- tibble(
  ID = c("Both F0", "F0 Female", "F0 Male", "Both Sexes Grand Offspring", "Female Grand Offspring", "Mal
  lnRR = c(All_Data_Analysis_f0$b[1],All_Data_Analysis_f0$b[2],All_Data_Analysis_f0$b[3],All_Data_Analys
  ci.lb = c(All_Data_Analysis_f0$ci.lb[1],All_Data_Analysis_f0$ci.lb[2],All_Data_Analysis_f0$ci.lb[3],Al
  ci.ub = c(All_Data_Analysis_f0$ci.ub[1],All_Data_Analysis_f0$ci.ub[2],All_Data_Analysis_f0$ci.ub[3],Al
)


plot_lnRR_overall_mods_f0_sex <- ggplot(Overall_effects_not_split_f0_sex, aes(x=ID, y=lnRR))+
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = ID, y = lnRR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "ID", y = "lnRR") +
  coord_flip()

plot_lnRR_overall_mods_f0_sex
```
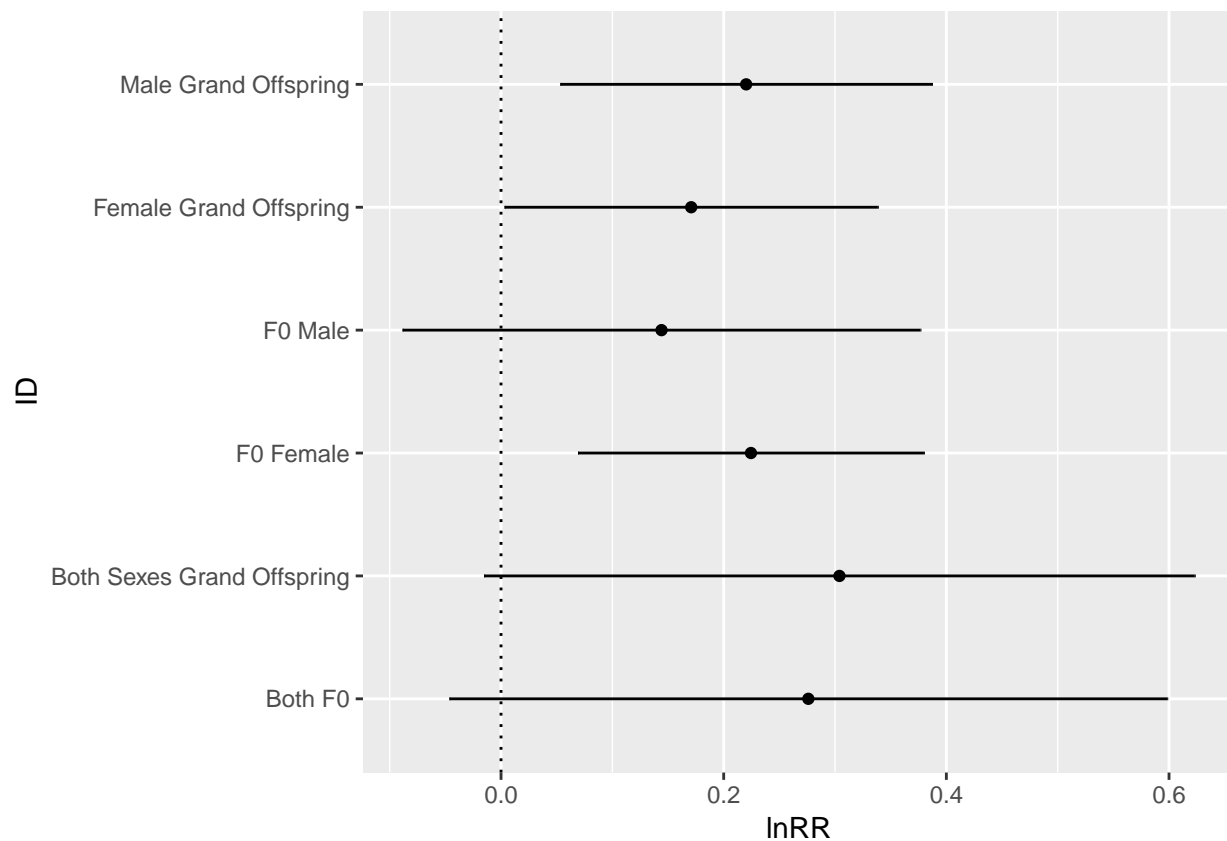
Meta-analysis with subsetted dataset (MG and OF exposure type)

```
#Overall analysis split by exposure type
All_Data_Analysis_MG <- rma.mv(yi, vi, random = list(~1|Trait, ~1|Paper_ID,~1|Cohort_ID,~1|ES_ID), data=

summary(All_Data_Analysis_MG)
```

```
##
## Multivariate Meta-Analysis Model (k = 118; method: REML)
##
##   logLik  Deviance       AIC       BIC      AICc
## -71.4877  142.9754  152.9754  166.7863  153.5160
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0843  0.2903      8     no      Trait
## sigma^2.2  0.1601  0.4001     13     no    Paper_ID
## sigma^2.3  0.0000  0.0000     24     no   Cohort_ID
## sigma^2.4  0.0790  0.2811    118     no      ES_ID
##
## Test for Heterogeneity:
## Q(df = 117) = 5726.1223, p-val < .0001
##
## Model Results:
##
## estimate       se     zval     pval    ci.lb    ci.ub
```
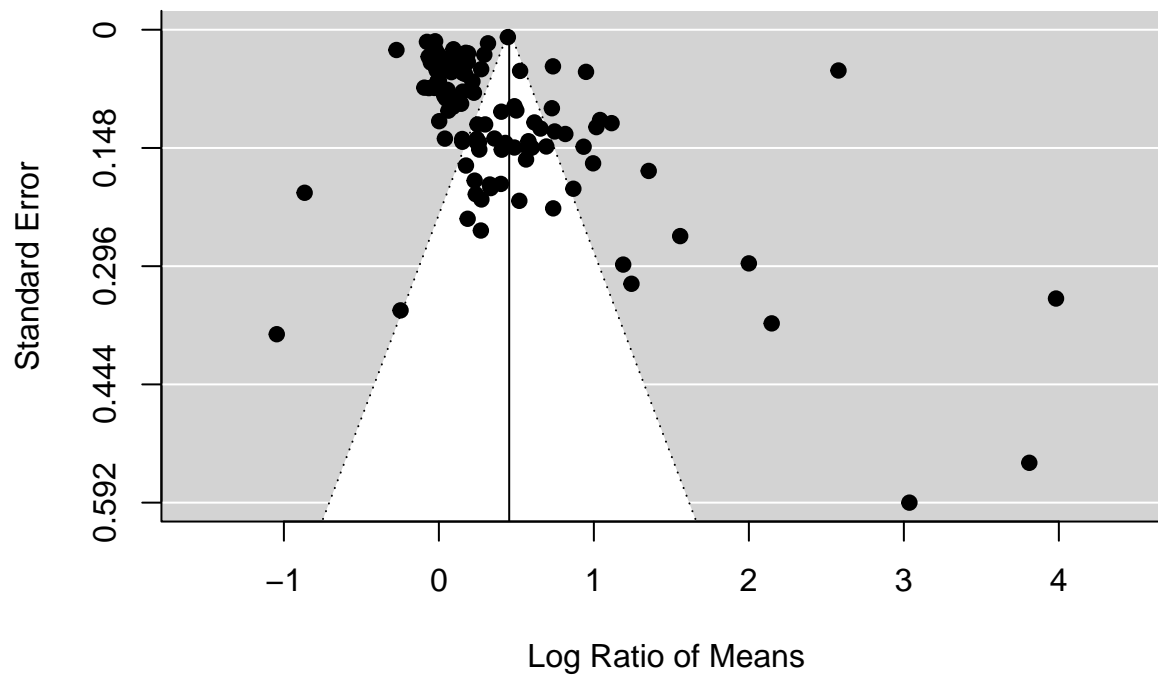
```
##    0.4537  0.1586  2.8601  0.0042  0.1428  0.7646  **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
funnel(All_Data_Analysis_MG)
```



```r
All_Data_Analysis_OF <- rma.mv(yi, vi, random = list(~1|Trait, ~1|Paper_ID,~1|Cohort_ID,~1|ES_ID), data=
```

```r
summary(All_Data_Analysis_OF)
```

```
##
## Multivariate Meta-Analysis Model (k = 223; method: REML)
##
##     logLik   Deviance        AIC        BIC        AICc
##   128.7990  -257.5981  -247.5981  -230.5847  -247.3203
##
## Variance Components:
##
##              estim    sqrt  nlvls  fixed      factor
## sigma^2.1   0.0026  0.0507      8     no       Trait
## sigma^2.2   0.0020  0.0444     16     no    Paper_ID
## sigma^2.3   0.0009  0.0301     53     no   Cohort_ID
## sigma^2.4   0.0006  0.0255    223     no       ES_ID
##
```

```
## Test for Heterogeneity:
## Q(df = 222) = 552.2364, p-val < .0001
##
## Model Results:
##
## estimate      se    zval    pval   ci.lb   ci.ub
##   0.0648  0.0246  2.6346  0.0084  0.0166  0.1129  **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Data_Analysis_OF)
```
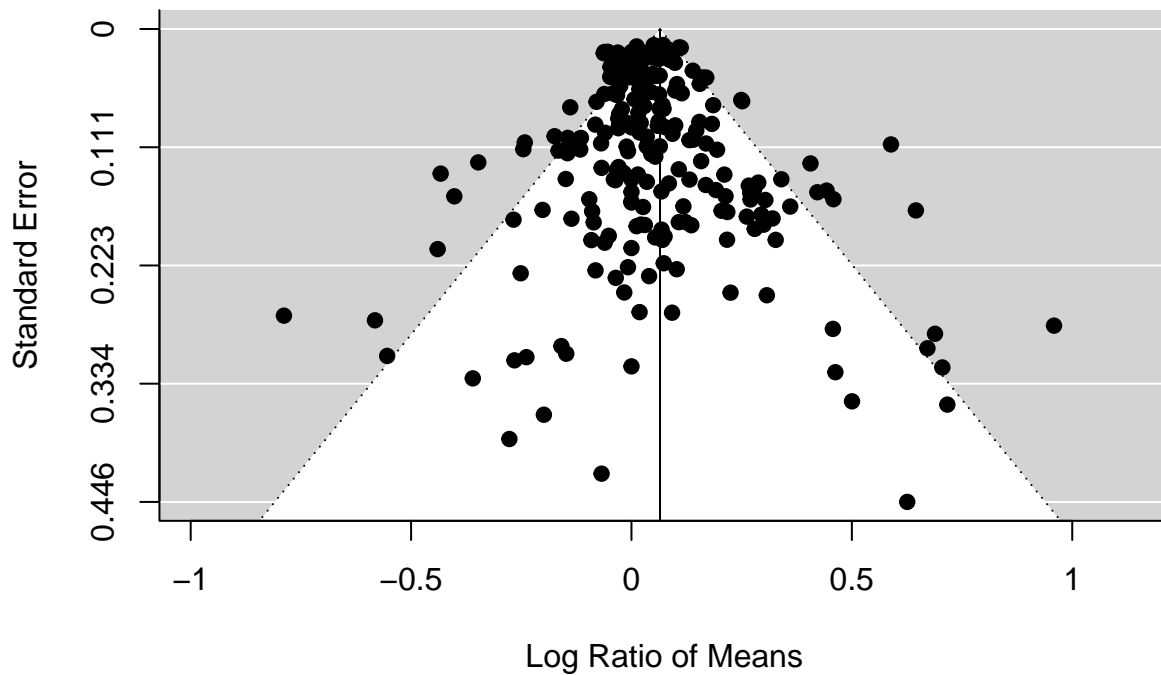


```
Overall_Exp_lnRR <- tibble(
  Exposure_Type = c("Multigenerational", "One off"),
  lnRR = c(0.4537,0.0662),
  ci.lb = c(0.1428,0.0199),
  ci.ub = c(0.7646,0.1126),
  k = c(118,223)
)
Overall_Exp_lnRR
```

```
## # A tibble: 2 x 5
##   Exposure_Type      lnRR  ci.lb ci.ub     k
##   <chr>             <dbl>  <dbl> <dbl> <dbl>
```

```
## 1 Multigenerational 0.454  0.143  0.765    118
## 2 One off           0.0662 0.0199 0.113    223
```

```
plot_lnRR_overall_exp <- ggplot(Overall_Exp_lnRR, aes(x=Exposure_Type, y=lnRR, colour=Exposure_Type)) +
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = Exposure_Type, y = lnRR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "Exposure_Type", y = "lnRR") +
  coord_flip()
plot_lnRR_overall_exp
```
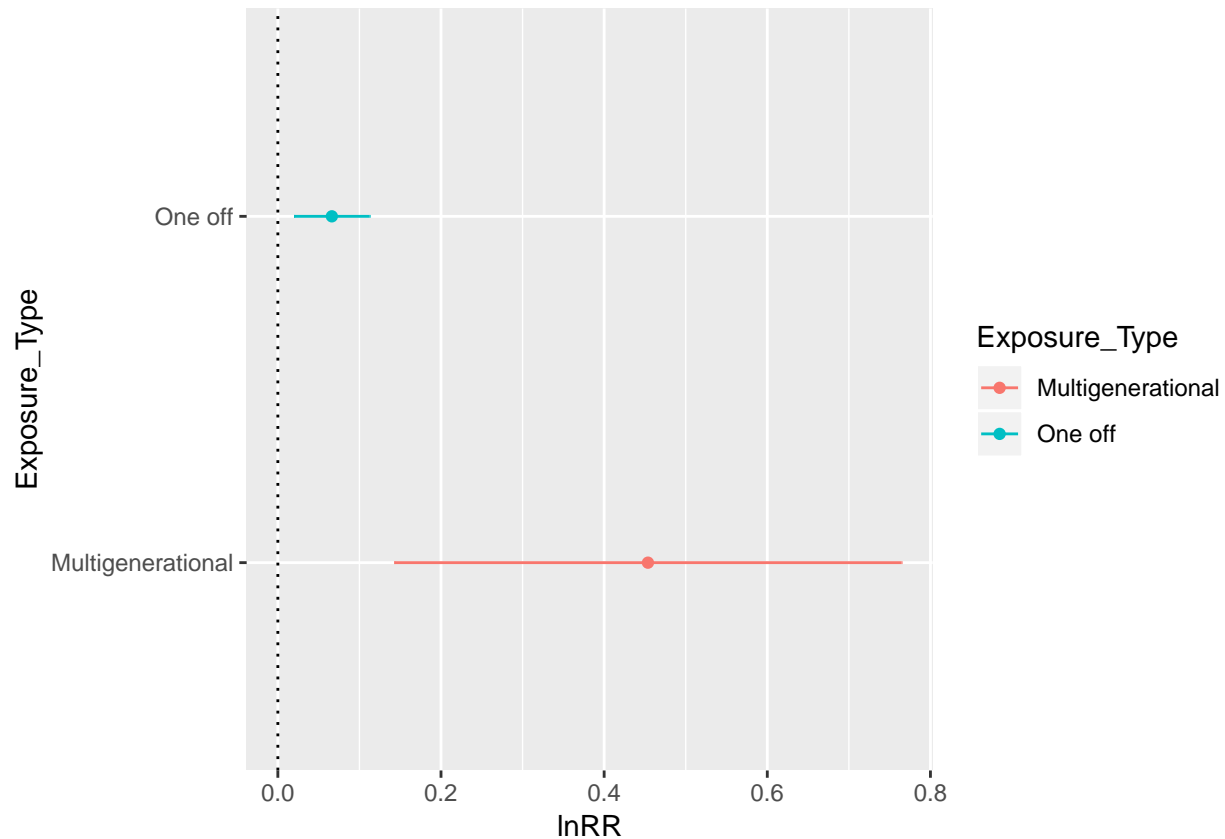


```
#Overall analysis with moderators (by exposure type)
Traits_Analysis_MG <- rma.mv(yi, vi, mods = ~Trait-1, random = list( ~1|Paper_ID,~1|Cohort_ID,~1|ES_ID)

summary(Traits_Analysis_MG)
```

```
##
## Multivariate Meta-Analysis Model (k = 118; method: REML)
##
##   logLik  Deviance      AIC       BIC      AICc
## -61.4207  122.8414  144.8414  174.5467  147.5353
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed    factor
```

```
## sigma^2.1  0.1544  0.3929     13     no    Paper_ID
## sigma^2.2  0.0000  0.0000     24     no   Cohort_ID
## sigma^2.3  0.0826  0.2873    118     no      ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 110) = 3957.7227, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:8):
## QM(df = 8) = 78.0581, p-val < .0001
##
## Model Results:
##
##                    estimate      se    zval    pval    ci.lb   ci.ub
## TraitAdiposity       0.8702  0.1412  6.1611  <.0001   0.5933  1.1470  ***
## TraitBody_Weight     0.1825  0.1209  1.5098  0.1311  -0.0544  0.4195
## TraitGlucose_FBG     0.1332  0.1615  0.8247  0.4095  -0.1833  0.4497
## TraitGlucose_TT      0.2208  0.1600  1.3804  0.1675  -0.0927  0.5343
## TraitInsulin_FI      0.6425  0.1897  3.3875  0.0007   0.2708  1.0142  ***
## TraitInsulin_TT      0.2695  0.1659  1.6245  0.1043  -0.0557  0.5947
## TraitLeptin          0.9215  0.1810  5.0899  <.0001   0.5666  1.2763  ***
## TraitTriglycerides   0.4817  0.1768  2.7244  0.0064   0.1352  0.8282   **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
k_traits_MG <- MG_ALL %>% group_by(Trait) %>% count()
k_traits_MG
```

```
## # A tibble: 8 x 2
## # Groups:   Trait [8]
##   Trait             n
##   <fct>         <int>
## 1 Adiposity        19
## 2 Body_Weight      52
## 3 Glucose_FBG       8
## 4 Glucose_TT        9
## 5 Insulin_FI        7
## 6 Insulin_TT        9
## 7 Leptin            7
## 8 Triglycerides     7
```

```r
Traits_Analysis_OF <- rma.mv(yi, vi, mods = ~Trait-1, random = list( ~1|Paper_ID,~1|Cohort_ID,~1|ES_ID)

summary(Traits_Analysis_OF)
```

```
##
## Multivariate Meta-Analysis Model (k = 223; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
##   128.9981  -257.9962  -235.9962  -198.9192  -234.6957
##
## Variance Components:
##
```

```
##              estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0019  0.0440     16     no    Paper_ID
## sigma^2.2  0.0009  0.0301     53     no   Cohort_ID
## sigma^2.3  0.0006  0.0251    223     no       ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 215) = 519.3353, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:8):
## QM(df = 8) = 43.0132, p-val < .0001
##
## Model Results:
##
##                      estimate      se     zval    pval    ci.lb   ci.ub
## TraitAdiposity         0.1163  0.0299   3.8852  0.0001   0.0576  0.1749
## TraitBody_Weight       0.0224  0.0143   1.5667  0.1172  -0.0056  0.0505
## TraitGlucose_FBG       0.0788  0.0430   1.8320  0.0670  -0.0055  0.1631
## TraitGlucose_TT        0.0223  0.0243   0.9170  0.3591  -0.0253  0.0698
## TraitInsulin_FI        0.0939  0.0390   2.4052  0.0162   0.0174  0.1703
## TraitInsulin_TT       -0.0383  0.0381  -1.0044  0.3152  -0.1131  0.0364
## TraitLeptin            0.1597  0.0588   2.7160  0.0066   0.0445  0.2750
## TraitTriglycerides     0.1125  0.0266   4.2365  <.0001   0.0605  0.1646
##
## TraitAdiposity        ***
## TraitBody_Weight
## TraitGlucose_FBG        .
## TraitGlucose_TT
## TraitInsulin_FI         *
## TraitInsulin_TT
## TraitLeptin            **
## TraitTriglycerides    ***
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
k_traits_OF <- OF_ALL %>% group_by(Trait) %>% count()
k_traits_OF
```

```
## # A tibble: 8 x 2
## # Groups:   Trait [8]
##   Trait           n
##   <fct>       <int>
## 1 Adiposity      46
## 2 Body_Weight    94
## 3 Glucose_FBG     4
## 4 Glucose_TT     19
## 5 Insulin_FI     19
## 6 Insulin_TT     10
## 7 Leptin          5
## 8 Triglycerides  26
```

```r
Traits_analysis_Exp <- tibble(
  Exposure_Type = c("Multigenerational","Multigenerational","Multigenerational","Multigenerational","Mul
```

```
Trait = c("Adiposity", "Body Weight", "Glucose_FBG","Glucose_TT", "Insulin_FI", "Insulin_TT","Leptin"
lnRR = c(0.8702,0.1825,0.1332,0.2208,0.6425,0.2695,0.9215,0.4817,0.1162,0.0223,0.0788,0.0220,0.0942,-0
ci.lb = c(0.5933,-0.0544,-0.1833,-0.0927,0.2708,-0.0557,0.5666,0.1352,0.0575,-0.0058,-0.0056,-0.0256,0
ci.ub = c(1.1470,0.4195,0.4497,0.5343,1.0142,0.5947,1.2763,0.8282,0.1749,0.0504,0.1633,0.0697,0.1707,0
k = c(k_traits_MG$n[1],k_traits_MG$n[2],k_traits_MG$n[3],k_traits_MG$n[4],k_traits_MG$n[5],k_traits_MG
)

plot_lnRR_overall_trait_exp <- ggplot(Traits_analysis_Exp, aes(x=Trait, y=lnRR, colour=Exposure_Type))
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = Trait, y = lnRR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "Exposure_Type", y = "lnRR") +
  coord_flip()
plot_lnRR_overall_trait_exp
```



```
#F0 and offspring sex analysis
All_Traits_Analysis_Omods_MG_f0 <- rma.mv(yi, vi, mods = ~F0_Parent_Exposed-1, random = list(~1|Trait,
```

```
## Warning in rma.mv(yi, vi, mods = ~F0_Parent_Exposed - 1, random = list(~1
## | : Redundant predictors dropped from the model.
```

```
summary(All_Traits_Analysis_Omods_MG_f0)
```
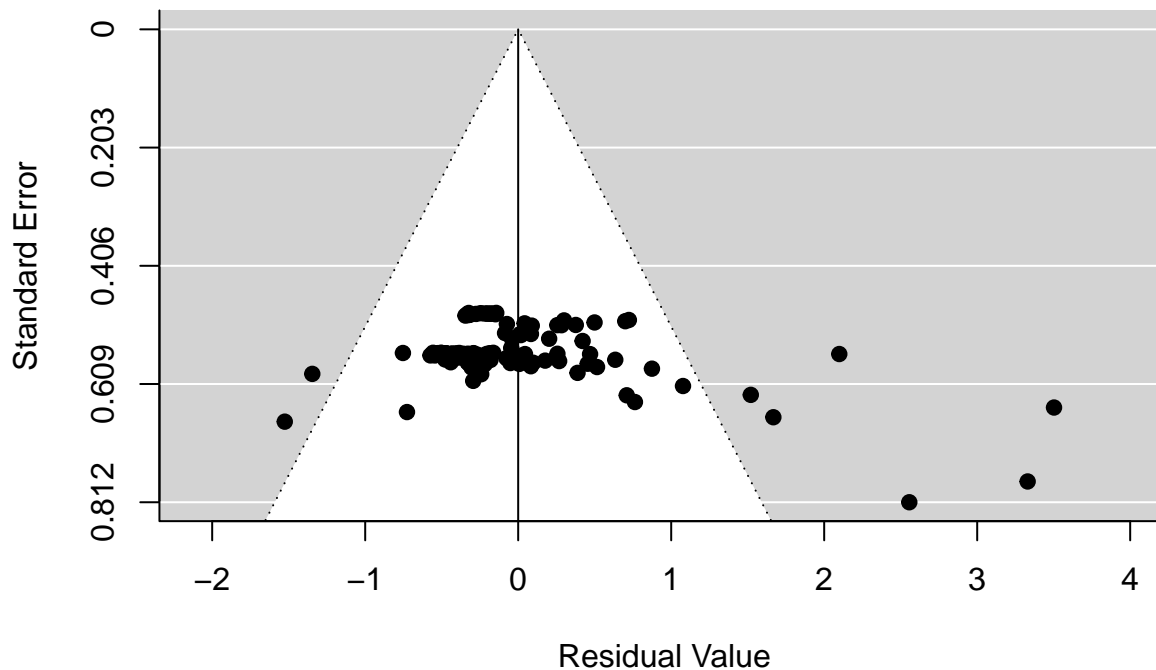
```
##
```

```
## Multivariate Meta-Analysis Model (k = 118; method: REML)
##
##    logLik  Deviance       AIC       BIC      AICc
## -69.9877  139.9755  151.9755  168.4970  152.7461
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0844  0.2904      8     no      Trait
## sigma^2.2  0.1735  0.4166     13     no    Paper_ID
## sigma^2.3  0.0000  0.0000     24     no   Cohort_ID
## sigma^2.4  0.0794  0.2818    118     no       ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 116) = 5697.9389, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:2):
## QM(df = 2) = 8.0483, p-val = 0.0179
##
## Model Results:
##
##                         estimate      se    zval    pval    ci.lb   ci.ub
## F0_Parent_ExposedFemale   0.4796  0.1710  2.8045  0.0050   0.1444  0.8148
## F0_Parent_ExposedMale     0.3166  0.3180  0.9956  0.3195  -0.3067  0.9400
##
## F0_Parent_ExposedFemale  **
## F0_Parent_ExposedMale
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_Omods_MG_f0)
```
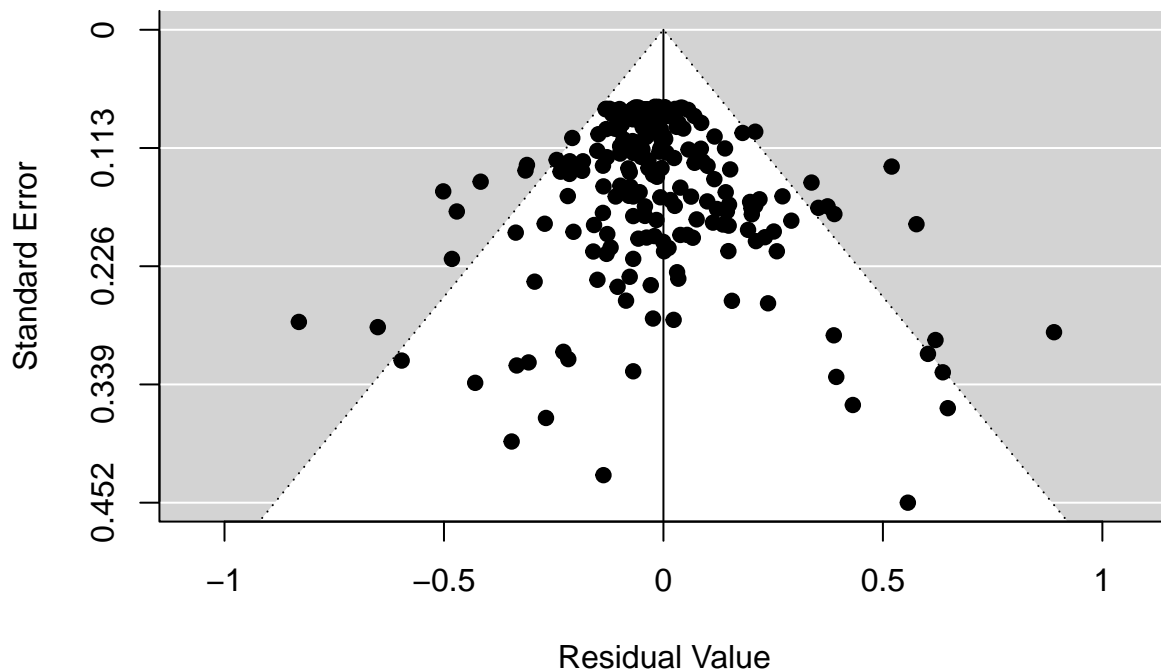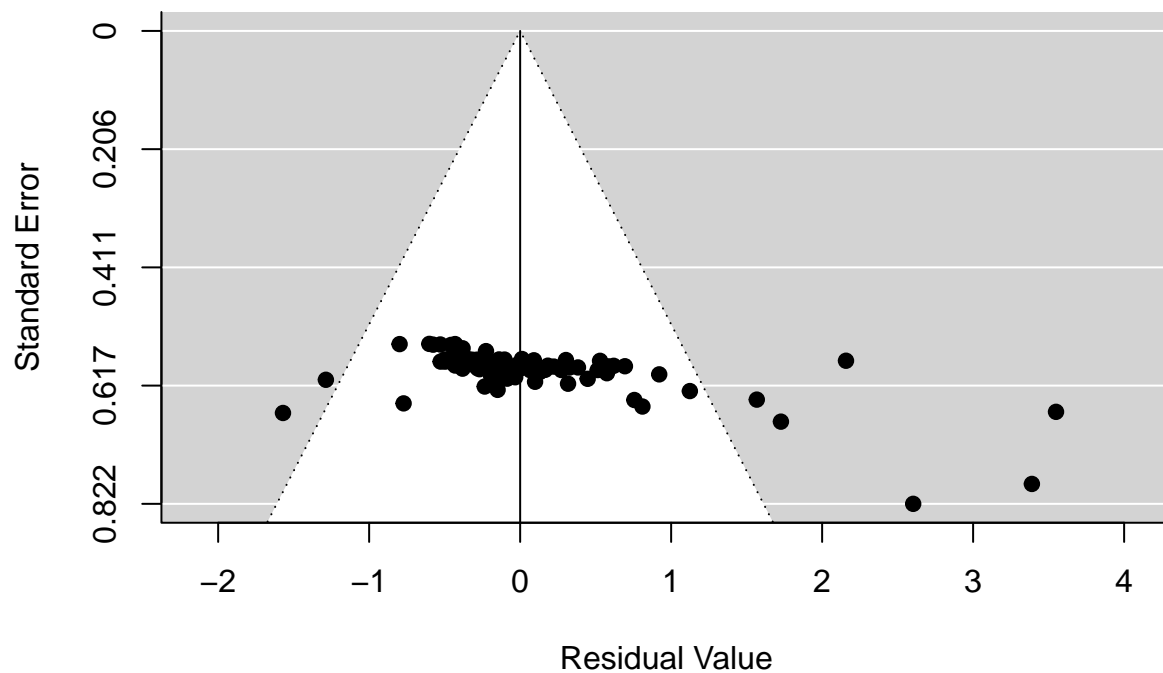
```
All_Traits_Analysis_Omods_OF_f0 <- rma.mv(yi, vi, mods = ~F0_Parent_Exposed-1, random = list(~1|Trait,

summary(All_Traits_Analysis_Omods_OF_f0)
```

```
##
## Multivariate Meta-Analysis Model (k = 223; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
##   131.0192  -262.0384  -248.0384  -224.2830  -247.5101
##
## Variance Components:
##
##              estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0026  0.0509      8     no      Trait
## sigma^2.2  0.0022  0.0466     16     no    Paper_ID
## sigma^2.3  0.0006  0.0244     53     no   Cohort_ID
## sigma^2.4  0.0005  0.0233    223     no       ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 220) = 529.0430, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:3):
## QM(df = 3) = 16.6218, p-val = 0.0008
##
## Model Results:
```

```
## 
##                       estimate      se     zval     pval    ci.lb    ci.ub
## F0_Parent_ExposedBoth    0.1817  0.0508   3.5777   0.0003   0.0821   0.2812
## F0_Parent_ExposedFemale  0.0688  0.0257   2.6819   0.0073   0.0185   0.1191
## F0_Parent_ExposedMale    0.0421  0.0325   1.2970   0.1946  -0.0215   0.1057
## 
## F0_Parent_ExposedBoth   ***
## F0_Parent_ExposedFemale  **
## F0_Parent_ExposedMale
## 
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
funnel(All_Traits_Analysis_0mods_OF_f0)
```



```r
All_Traits_Analysis_0mods_MG_sex <- rma.mv(yi, vi, mods = ~Sex-1, random = list(~1|Trait, ~1|Paper_ID,~
```

```r
summary(All_Traits_Analysis_0mods_MG_sex)
```

```
## 
## Multivariate Meta-Analysis Model (k = 118; method: REML)
## 
##    logLik  Deviance       AIC       BIC      AICc
## -70.8274  141.6548  155.6548  174.8693  156.7015
## 
```

```
## Variance Components:
##
##              estim    sqrt  nlvls  fixed      factor
## sigma^2.1   0.0848  0.2912      8     no       Trait
## sigma^2.2   0.1944  0.4409     13     no    Paper_ID
## sigma^2.3   0.0000  0.0000     24     no   Cohort_ID
## sigma^2.4   0.0797  0.2824    118     no       ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 115) = 5048.7974, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:3):
## QM(df = 3) = 7.4666, p-val = 0.0584
##
## Model Results:
##
##            estimate      se    zval    pval   ci.lb   ci.ub
## SexBoth      0.5247  0.2510  2.0904  0.0366  0.0327  1.0166  *
## SexFemale    0.4203  0.1806  2.3268  0.0200  0.0663  0.7743  *
## SexMale      0.4328  0.1832  2.3623  0.0182  0.0737  0.7918  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_0mods_MG_sex)
```

```
All_Traits_Analysis_0mods_OF_sex <- rma.mv(yi, vi, mods = ~Sex-1, random = list(~1|Trait, ~1|Paper_ID,~1

summary(All_Traits_Analysis_0mods_OF_sex)
```

```
##
## Multivariate Meta-Analysis Model (k = 223; method: REML)
##
##     logLik   Deviance        AIC        BIC        AICc
##   131.5220  -263.0441  -249.0441  -225.2887  -248.5158
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed      factor
## sigma^2.1  0.0020  0.0446      8     no       Trait
## sigma^2.2  0.0019  0.0439     16     no    Paper_ID
## sigma^2.3  0.0008  0.0289     53     no   Cohort_ID
## sigma^2.4  0.0007  0.0263    223     no       ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 220) = 538.0910, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:3):
## QM(df = 3) = 17.4113, p-val = 0.0006
##
## Model Results:
##
##             estimate      se     zval    pval    ci.lb    ci.ub
## SexBoth      -0.3567  0.1428  -2.4985  0.0125  -0.6366  -0.0769    *
## SexFemale     0.0632  0.0242   2.6110  0.0090   0.0158   0.1107   **
## SexMale       0.0755  0.0238   3.1646  0.0016   0.0287   0.1222   **
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_0mods_OF_sex)
```
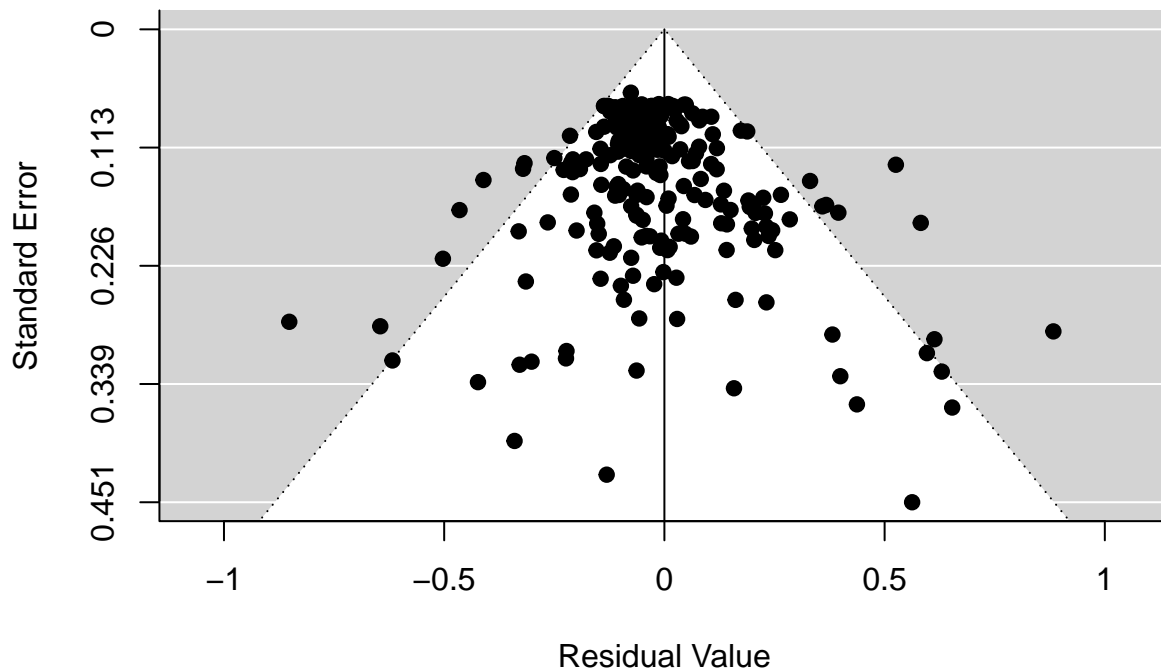
```
Overall_Exp_mods_lnRR <- tibble(
  Exposure_Type = c("Multigenerational","Multigenerational", "One off", "One off", "One off", "Multigen
  mod = c("F0 Female","F0 Male", "F0 Both", "F0 Female", "F0 Male","Both Offspring Sex","Female Offsprin
  lnRR = c(0.4796,0.3166,0.1833,0.0699,0.0435,0.5219,0.4147,0.4395,-0.3662,0.0645,0.0772),
  ci.lb = c(0.1444,-0.3067,0.0845,0.0212,-0.0189,0.0303,0.0600,0.0814,-0.6458,0.0179,0.0317),
  ci.ub = c(0.8148,0.9400,0.2820,0.1187,0.1059,1.0136,0.7695,0.7975,-0.0866,0.111,0.1226)
)

plot_lnRR_overall_mods_exp <- ggplot(Overall_Exp_mods_lnRR, aes(x=mod, y=lnRR, colour=Exposure_Type))+
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = mod, y = lnRR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "mod", y = "lnRR") +
  coord_flip()

plot_lnRR_overall_mods_exp
```
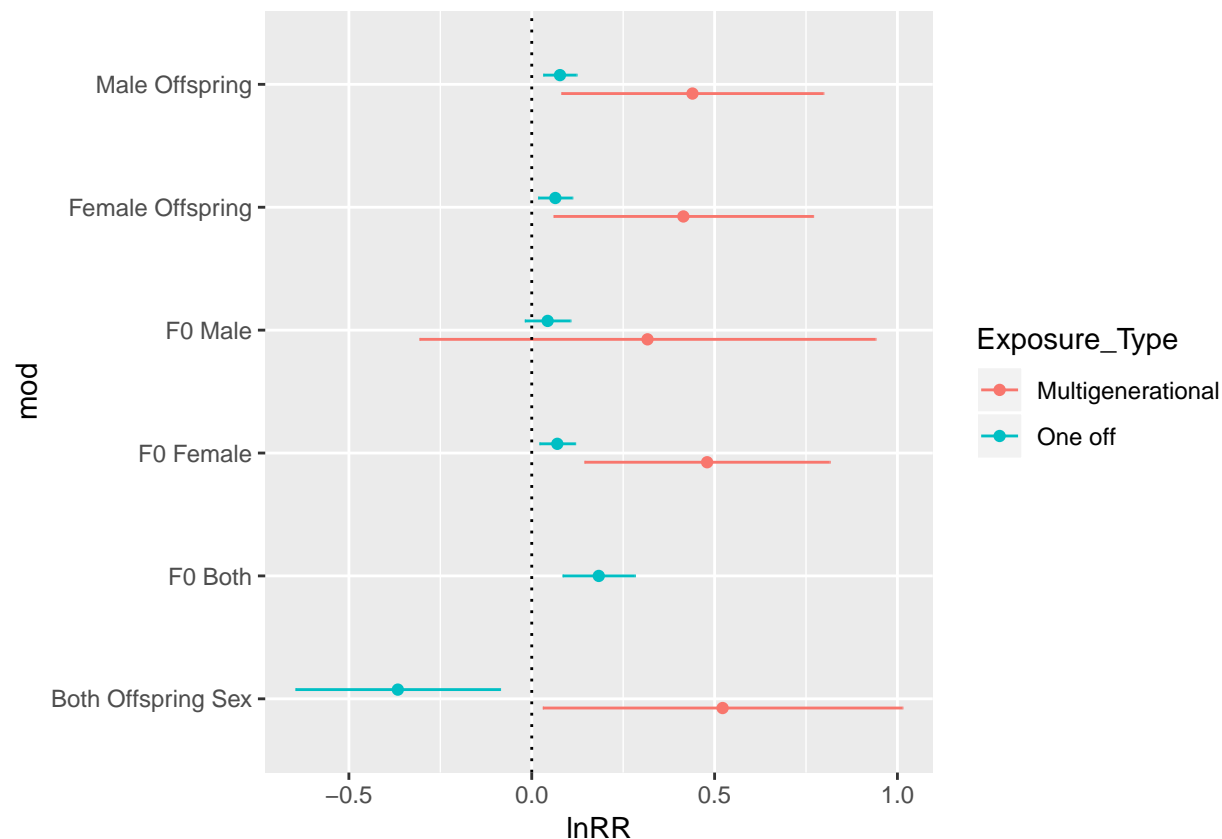
Meta-analysis overall results (lnCVR)

4. Calculating effect sizes (Done)

We calculated our effect sizes (lnCVR) for our complete data set (all traits).

5. Running meta-analysis for lnCVR

```
#Modelling entire dataset with no moderators

All_Traits_Analysis_Omods_lnCVR <- rma.mv(yi, vi, random = list(~1|Trait, ~1|Paper_ID,~1|Cohort_ID,~1|ES

summary(All_Traits_Analysis_Omods_lnCVR)
```

```
##
## Multivariate Meta-Analysis Model (k = 341; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -267.4073   534.8145   544.8145   563.9593   544.9942
##
## Variance Components:
##
##              estim    sqrt   nlvls   fixed      factor
## sigma^2.1   0.0176   0.1325       8      no       Trait
```

```
## sigma^2.2  0.0251  0.1583     25     no     Paper_ID
## sigma^2.3  0.0000  0.0000     75     no   Cohort_ID
## sigma^2.4  0.1093  0.3307    341     no        ES_ID
##
## Test for Heterogeneity:
## Q(df = 340) = 800.9658, p-val < .0001
##
## Model Results:
##
## estimate      se     zval     pval    ci.lb    ci.ub
##  -0.0579  0.0706  -0.8199   0.4123  -0.1961   0.0804
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```r
funnel(All_Traits_Analysis_0mods_lnCVR)
```
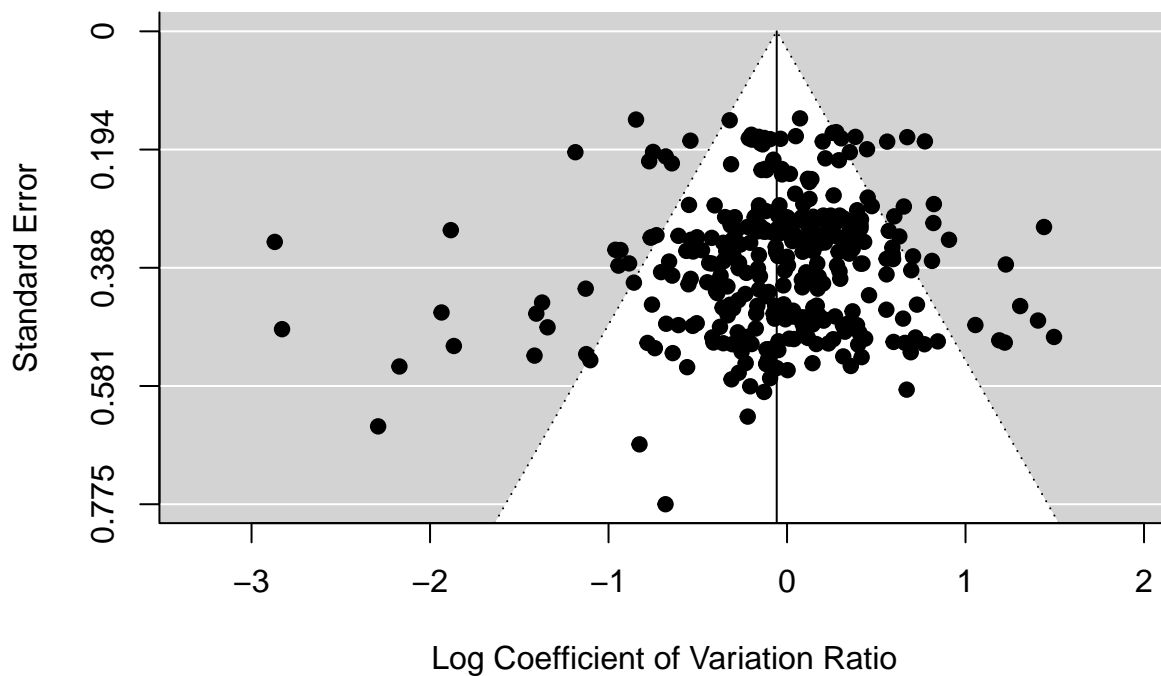


```r
Overall_lnCVR <- tibble(
  ID = "Overall",
  lnCVR = c(-0.0579),
  ci.lb = c(-0.1961),
  ci.ub = c(0.0804)
)
Overall_lnCVR
```

```
## # A tibble: 1 x 4
```

```
##    ID       lnCVR  ci.lb  ci.ub
##    <chr>     <dbl>  <dbl>  <dbl>
## 1 Overall -0.0579 -0.196 0.0804
```

```r
plot_lnRR_overall_lnCVR <- ggplot(Overall_lnCVR, aes(x=ID, y=lnCVR)) +
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = ID, y = lnCVR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "ID", y = "lnCVR") +
  coord_flip()
plot_lnRR_overall_lnCVR
```
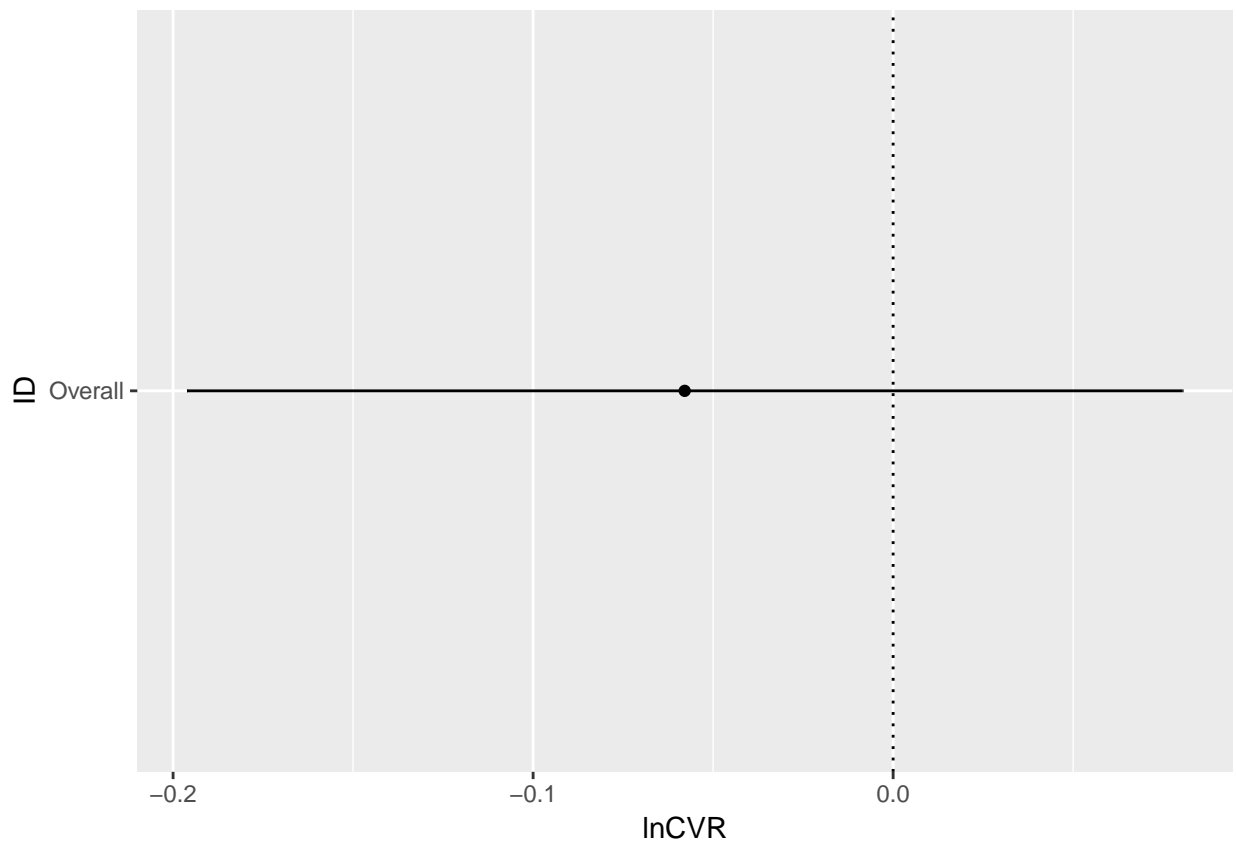

Modelling traits with overall dataset

```r
All_Traits_Analysis_traits_lnCVR <- rma.mv(yi, vi, mods= ~Trait-1, random = list(~1|Paper_ID,~1|Cohort_

summary(All_Traits_Analysis_traits_lnCVR)
```

```
##
## Multivariate Meta-Analysis Model (k = 341; method: REML)
##
##     logLik   Deviance        AIC        BIC        AICc
```

```
## -257.8572    515.7144    537.7144    579.6040    538.5368
##
## Variance Components:
##
##              estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0253  0.1590     25     no   Paper_ID
## sigma^2.2  0.0000  0.0000     75     no  Cohort_ID
## sigma^2.3  0.1095  0.3308    341     no      ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 333) = 762.1820, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:8):
## QM(df = 8) = 20.0331, p-val = 0.0102
##
## Model Results:
##
##                      estimate      se     zval    pval    ci.lb     ci.ub
## TraitAdiposity        -0.0610  0.0838  -0.7282  0.4665  -0.2254    0.1033
## TraitBody_Weight       0.0298  0.0540   0.5519  0.5810  -0.0760    0.1355
## TraitGlucose_FBG      -0.1652  0.1469  -1.1249  0.2606  -0.4531    0.1226
## TraitGlucose_TT        0.0992  0.1124   0.8830  0.3772  -0.1210    0.3195
## TraitInsulin_FI       -0.3983  0.1174  -3.3937  0.0007  -0.6284   -0.1683
## TraitInsulin_TT        0.2099  0.1417   1.4815  0.1385  -0.0678    0.4877
## TraitLeptin           -0.1094  0.1575  -0.6945  0.4874  -0.4180    0.1993
## TraitTriglycerides    -0.1040  0.1046  -0.9940  0.3202  -0.3090    0.1011
##
## TraitAdiposity
## TraitBody_Weight
## TraitGlucose_FBG
## TraitGlucose_TT
## TraitInsulin_FI      ***
## TraitInsulin_TT
## TraitLeptin
## TraitTriglycerides
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_traits_lnCVR)
```
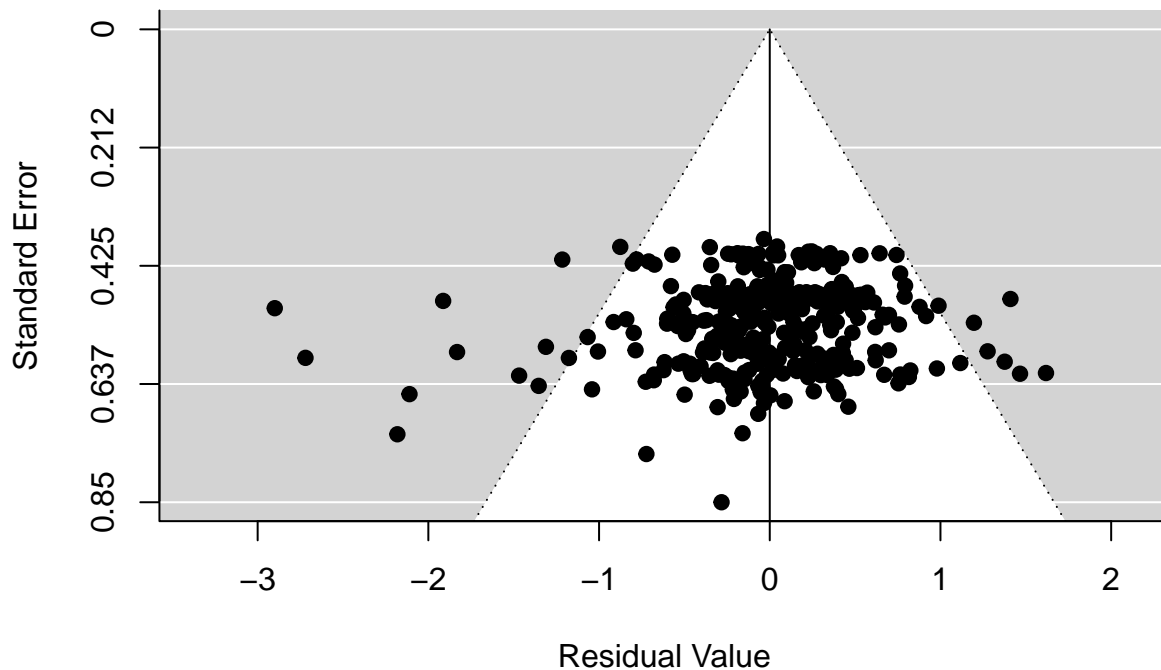
```
Traits_overall_lnCVR <- tibble(
  Trait = c("Adiposity", "Body Weight","Glucose", "Insulin", "Leptin", "Triglycerides"),
  lnCVR = c(-0.0107,0.0261,0.0143,-0.1468,0.0245,-0.0817),
  ci.lb = c(-0.1557,-0.0742,-0.1343,-0.3042,-0.2159,-0.2524),
  ci.ub = c(0.1343,0.1264,0.1629,0.0106,0.2648,0.0891)
)
Traits_overall_lnCVR
```

```
## # A tibble: 6 x 4
##   Trait           lnCVR   ci.lb   ci.ub
##   <chr>           <dbl>   <dbl>   <dbl>
## 1 Adiposity      -0.0107 -0.156  0.134
## 2 Body Weight     0.0261 -0.0742 0.126
## 3 Glucose         0.0143 -0.134  0.163
## 4 Insulin        -0.147  -0.304  0.0106
## 5 Leptin          0.0245 -0.216  0.265
## 6 Triglycerides  -0.0817 -0.252  0.0891
```

```
plot_lnRR_overall_traits_lnCVR <- ggplot(Traits_overall_lnCVR, aes(x=Trait, y=lnCVR, colour = Trait)) +
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = Trait, y = lnCVR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "Trait", y = "lnCVR") +
  coord_flip()
plot_lnRR_overall_traits_lnCVR
```
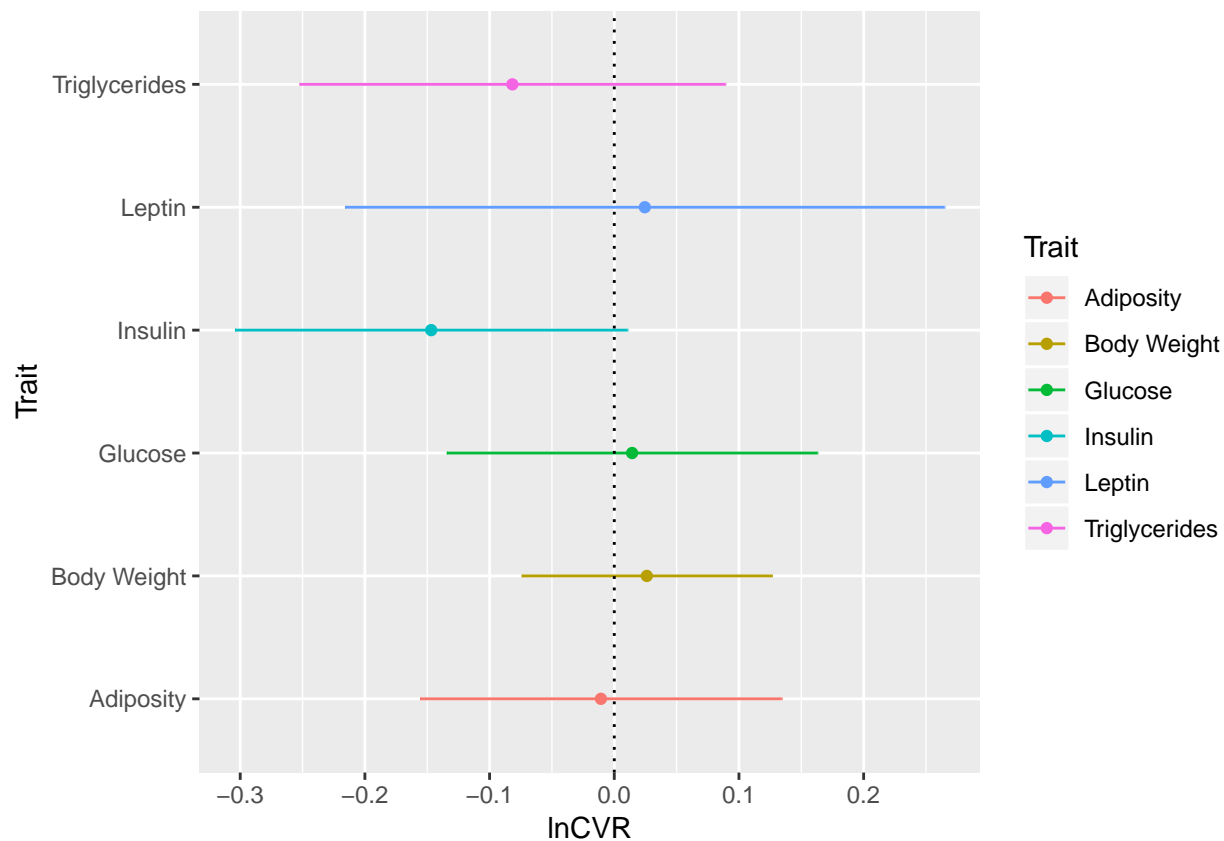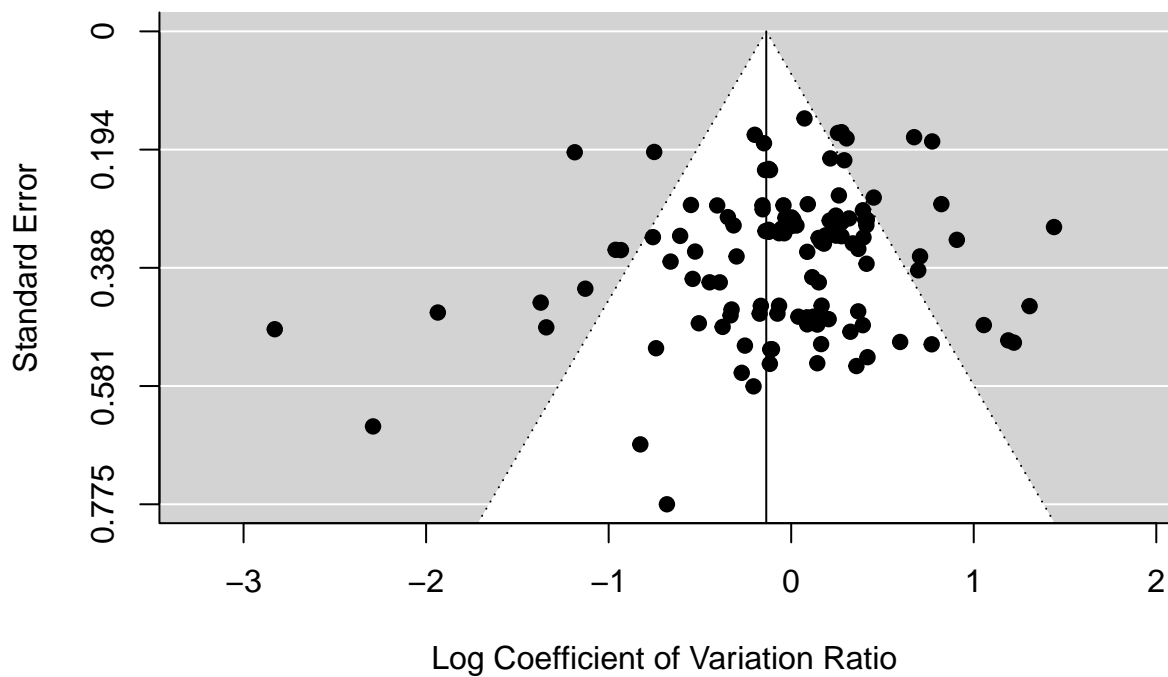
Modelling MG and OF (no mods) (lnCVR)

```
All_Data_Analysis_Omods_MG_lnCVR <- rma.mv(yi, vi, random = list(~1|Trait, ~1|Paper_ID,~1|Cohort_ID,~1|

summary(All_Data_Analysis_Omods_MG_lnCVR)
```

```
##
## Multivariate Meta-Analysis Model (k = 118; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -101.4081   202.8163   212.8163   226.6272   213.3568
##
## Variance Components:
##
##              estim     sqrt  nlvls  fixed      factor
## sigma^2.1   0.0542   0.2328      8     no       Trait
## sigma^2.2   0.0000   0.0000     13     no    Paper_ID
## sigma^2.3   0.0000   0.0000     24     no   Cohort_ID
## sigma^2.4   0.1499   0.3871    118     no       ES_ID
##
## Test for Heterogeneity:
## Q(df = 117) = 330.3777, p-val < .0001
##
```

```
## Model Results:
##
## estimate      se     zval    pval    ci.lb   ci.ub
##  -0.1366  0.1035  -1.3206  0.1866  -0.3394  0.0662
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Data_Analysis_0mods_MG_lnCVR)
```



```
All_Data_Analysis_0mods_OF_lnCVR <- rma.mv(yi, vi, random = list(~1|Trait, ~1|Paper_ID,~1|Cohort_ID,~1|
```

```
summary(All_Data_Analysis_0mods_OF_lnCVR)
```

```
##
## Multivariate Meta-Analysis Model (k = 223; method: REML)
##
##     logLik   Deviance       AIC       BIC       AICc
## -161.0005   322.0010   332.0010   349.0144   332.2788
##
## Variance Components:
##
##                estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0190  0.1379      8     no       Trait
## sigma^2.2  0.0317  0.1780     16     no     Paper_ID
```

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```
## sigma^2.3  0.0026  0.0509      53      no  Cohort_ID
## sigma^2.4  0.0778  0.2789     223      no     ES_ID
##
## Test for Heterogeneity:
## Q(df = 222) = 464.7551, p-val < .0001
##
## Model Results:
##
## estimate      se     zval    pval    ci.lb    ci.ub
##  -0.0104  0.0840  -0.1242  0.9011  -0.1751   0.1542
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Data_Analysis_Omods_OF_lnCVR)
```
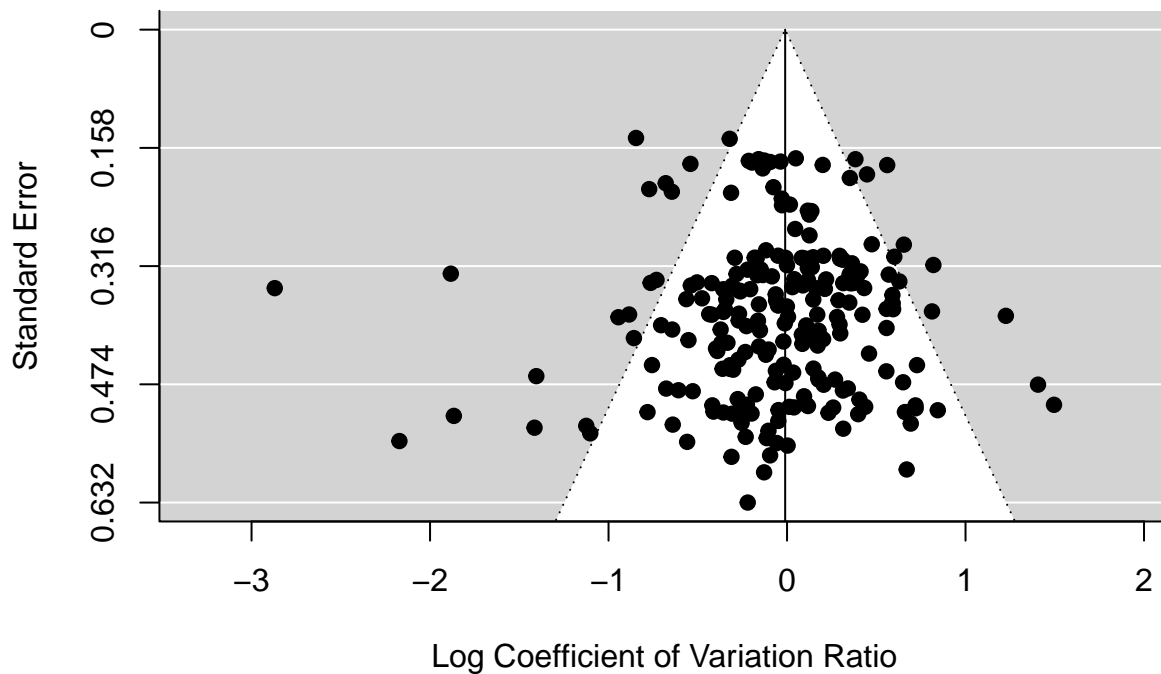


```
Exp_overall_lnCVR <- tibble(
  Exposure_Type = c("Multigenerational", "One off"),
  lnCVR = c(-0.1366,-0.1366),
  ci.lb = c(-0.3394,-0.3394),
  ci.ub = c(0.0662,0.0662)
)
Exp_overall_lnCVR
```

```
## # A tibble: 2 x 4
```

```
##    Exposure_Type       lnCVR  ci.lb  ci.ub
##    <chr>               <dbl>  <dbl>  <dbl>
## 1 Multigenerational  -0.137 -0.339 0.0662
## 2 One off            -0.137 -0.339 0.0662
```

```
plot_lnRR_overall_exp_lnCVR <- ggplot(Exp_overall_lnCVR, aes(x=Exposure_Type, y=lnCVR, colour = Exposur
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = Exposure_Type, y = lnCVR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "Exposure_Type", y = "lnCVR") +
  coord_flip()
plot_lnRR_overall_exp_lnCVR
```
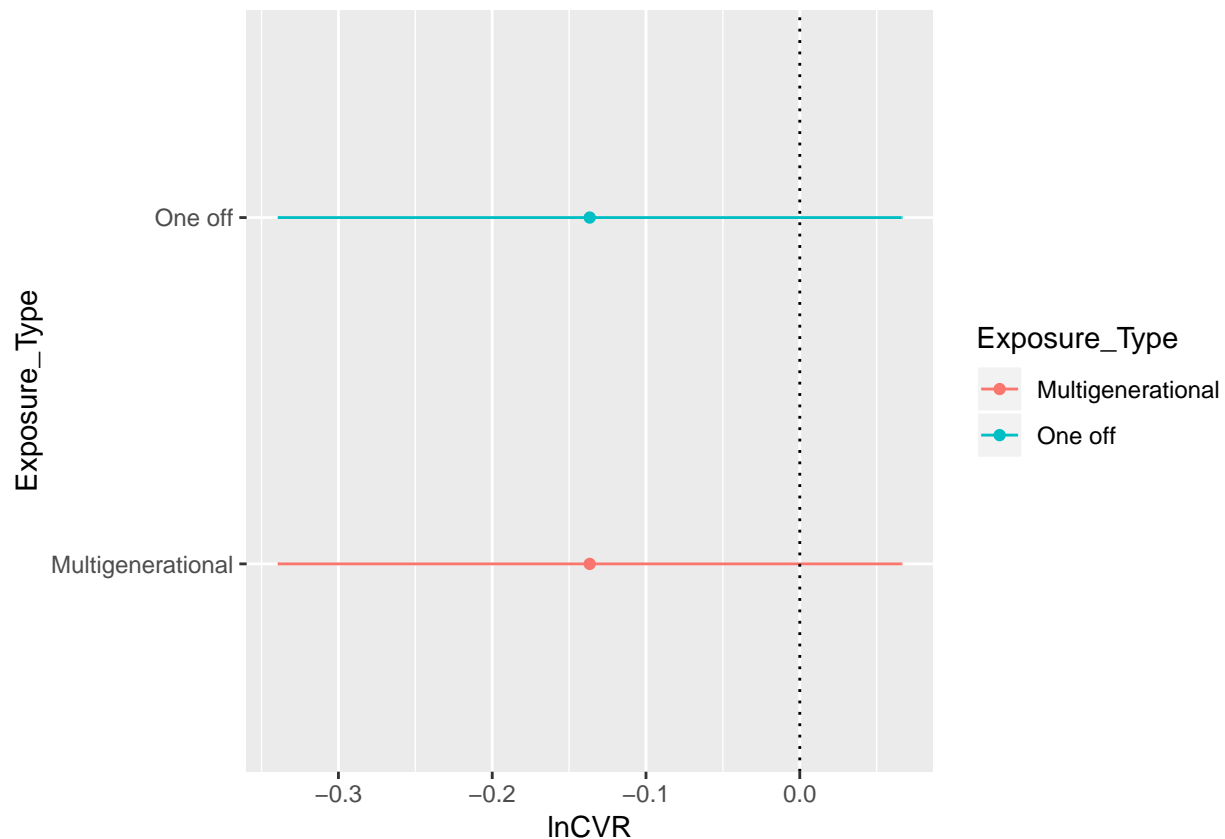

Modelling all traits split by MG and OF (lnCVR)

```
All_Traits_Analysis_MG_lnCVR <- rma.mv(yi, vi, mods= ~Trait-1, random = list(~1|Paper_ID,~1|Cohort_ID,~

summary(All_Traits_Analysis_MG_lnCVR)
```
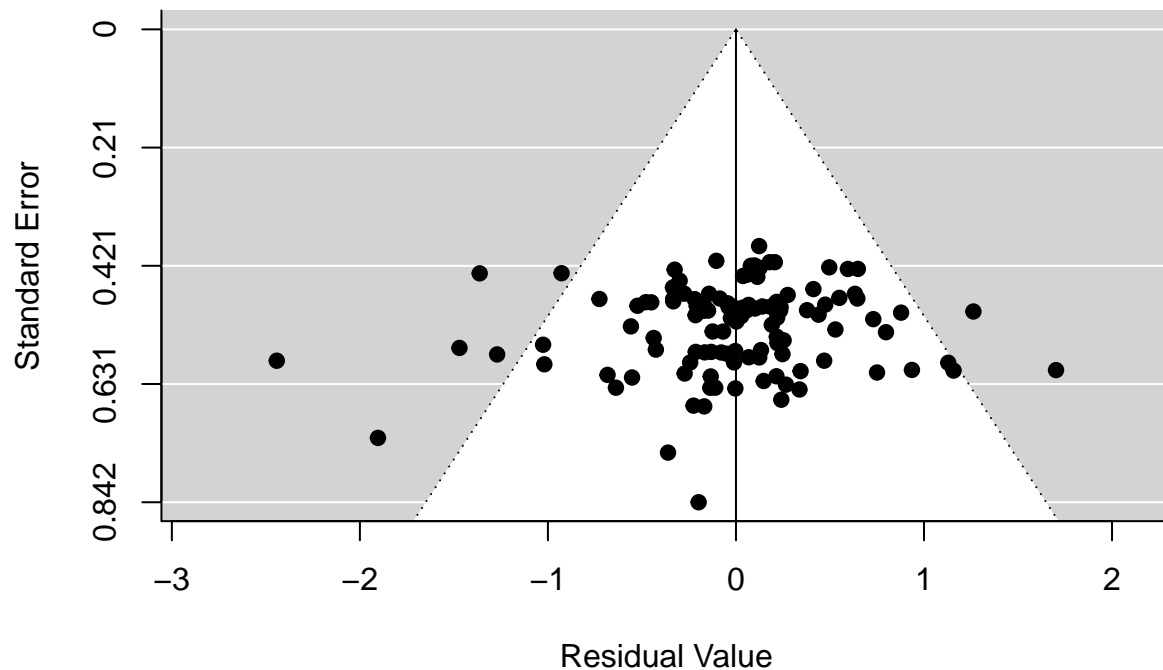
```
##
## Multivariate Meta-Analysis Model (k = 118; method: REML)
##
```

```
##    logLik  Deviance       AIC       BIC      AICc
## -91.8355  183.6709  205.6709  235.3762  208.3648
##
## Variance Components:
##
##             estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0000  0.0000     13     no   Paper_ID
## sigma^2.2  0.0000  0.0000     24     no  Cohort_ID
## sigma^2.3  0.1541  0.3925    118     no      ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 110) = 280.3182, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:8):
## QM(df = 8) = 24.9878, p-val = 0.0016
##
## Model Results:
##
##                      estimate      se     zval    pval    ci.lb    ci.ub
## TraitAdiposity        -0.1021  0.1301  -0.7851  0.4324  -0.3570   0.1528
## TraitBody_Weight       0.1770  0.0688   2.5744  0.0100   0.0422   0.3118  *
## TraitGlucose_FBG      -0.3227  0.1844  -1.7505  0.0800  -0.6840   0.0386  .
## TraitGlucose_TT        0.0195  0.2099   0.0930  0.9259  -0.3920   0.4310
## TraitInsulin_FI       -0.4823  0.2156  -2.2369  0.0253  -0.9048  -0.0597  *
## TraitInsulin_TT        0.2532  0.2078   1.2185  0.2230  -0.1541   0.6604
## TraitLeptin           -0.3871  0.2111  -1.8338  0.0667  -0.8007   0.0266  .
## TraitTriglycerides    -0.4652  0.2119  -2.1953  0.0281  -0.8806  -0.0499  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_MG_lnCVR)
```

```r
All_Traits_Analysis_OF_lnCVR <- rma.mv(yi, vi, mods= ~Trait-1, random = list(~1|Paper_ID,~1|Cohort_ID,~
summary(All_Traits_Analysis_OF_lnCVR)
```

```
##
## Multivariate Meta-Analysis Model (k = 223; method: REML)
##
##    logLik   Deviance        AIC        BIC       AICc
## -152.5181   305.0362   327.0362   364.1132   328.3367
##
## Variance Components:
##
##             estim     sqrt   nlvls   fixed      factor
## sigma^2.1  0.0344   0.1855      16      no    Paper_ID
## sigma^2.2  0.0025   0.0497      53      no   Cohort_ID
## sigma^2.3  0.0769   0.2773     223      no       ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 215) = 439.4961, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:8):
## QM(df = 8) = 15.5942, p-val = 0.0486
##
## Model Results:
##
```

```
##                     estimate      se     zval    pval   ci.lb    ci.ub
## TraitAdiposity       -0.0602  0.1023  -0.5884  0.5563  -0.2606   0.1403
## TraitBody_Weight     -0.0453  0.0699  -0.6478  0.5171  -0.1822   0.0917
## TraitGlucose_FBG      0.1297  0.2386   0.5437  0.5867  -0.3379   0.5974
## TraitGlucose_TT       0.1546  0.1281   1.2068  0.2275  -0.0965   0.4056
## TraitInsulin_FI      -0.3955  0.1327  -2.9801  0.0029  -0.6556  -0.1354
## TraitInsulin_TT       0.2362  0.1821   1.2969  0.1947  -0.1208   0.5931
## TraitLeptin           0.1853  0.2243   0.8263  0.4086  -0.2542   0.6249
## TraitTriglycerides   -0.0100  0.1173  -0.0851  0.9322  -0.2399   0.2199
##
## TraitAdiposity
## TraitBody_Weight
## TraitGlucose_FBG
## TraitGlucose_TT
## TraitInsulin_FI       **
## TraitInsulin_TT
## TraitLeptin
## TraitTriglycerides
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_OF_lnCVR)
```
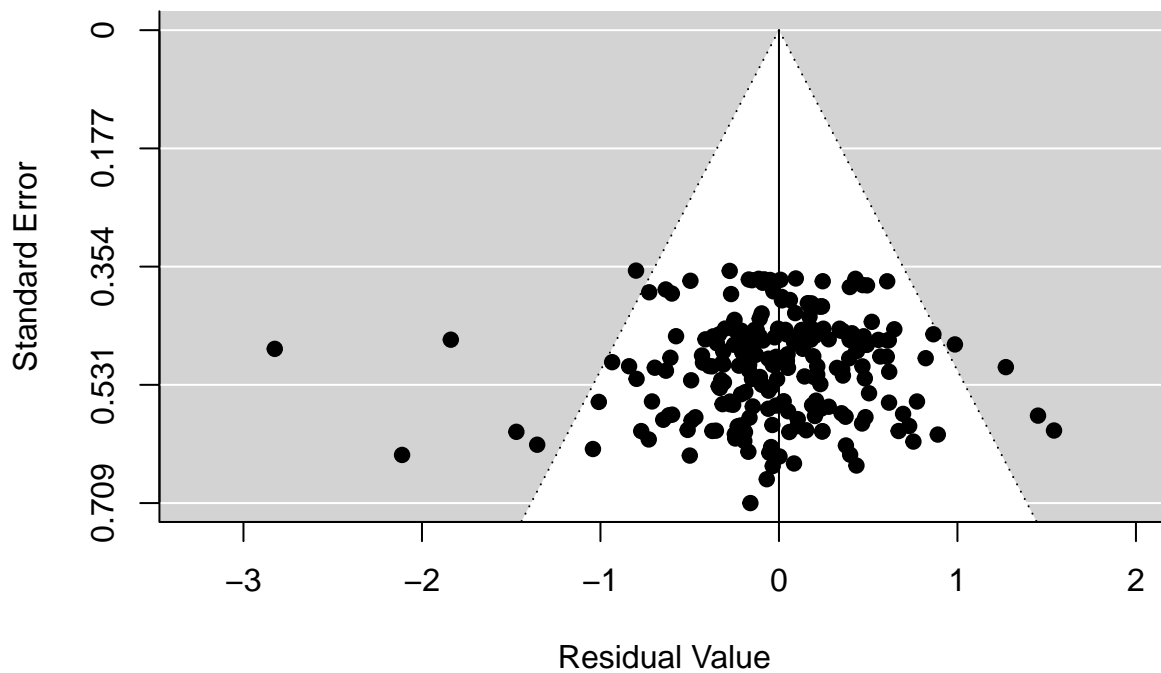
```
Traits_analysis_Exp_lnCVR <- tibble(
  Exposure_Type = c("Multigenerational","Multigenerational","Multigenerational","Multigenerational","Mul
  Trait = c("Adiposity", "Body Weight", "Glucose_FBG","Glucose_TT", "Insulin_FI", "Insulin_TT","Leptin"
  lnRR = c(-0.1021,0.1770,-0.3227,0.0195,-0.4823,0.2532,-0.387,-0.4652,-0.0602,-0.0451,0.1298,0.1545,-0
  ci.lb = c(-0.3570,0.0422,-0.6840,-0.3920,-0.9048,-0.1541,-0.8007,-0.8806,-0.2606,-0.1821,-0.3384,-0.09
  ci.ub = c(0.1528,0.3118,0.0386,0.4310,-0.0597,0.6604,0.0266,-0.0499,0.1402,0.0919,0.5981,0.4056,-0.135
  k = c(k_traits_MG$n[1],k_traits_MG$n[2],k_traits_MG$n[3],k_traits_MG$n[4],k_traits_MG$n[5],k_traits_MG
)

plot_lnRR_overall_trait_exp_lnCVR <- ggplot(Traits_analysis_Exp_lnCVR, aes(x=Trait, y=lnRR, colour=Expos
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = Trait, y = lnRR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "Exposure_Type", y = "lnRR") +
  coord_flip()
plot_lnRR_overall_trait_exp_lnCVR
```
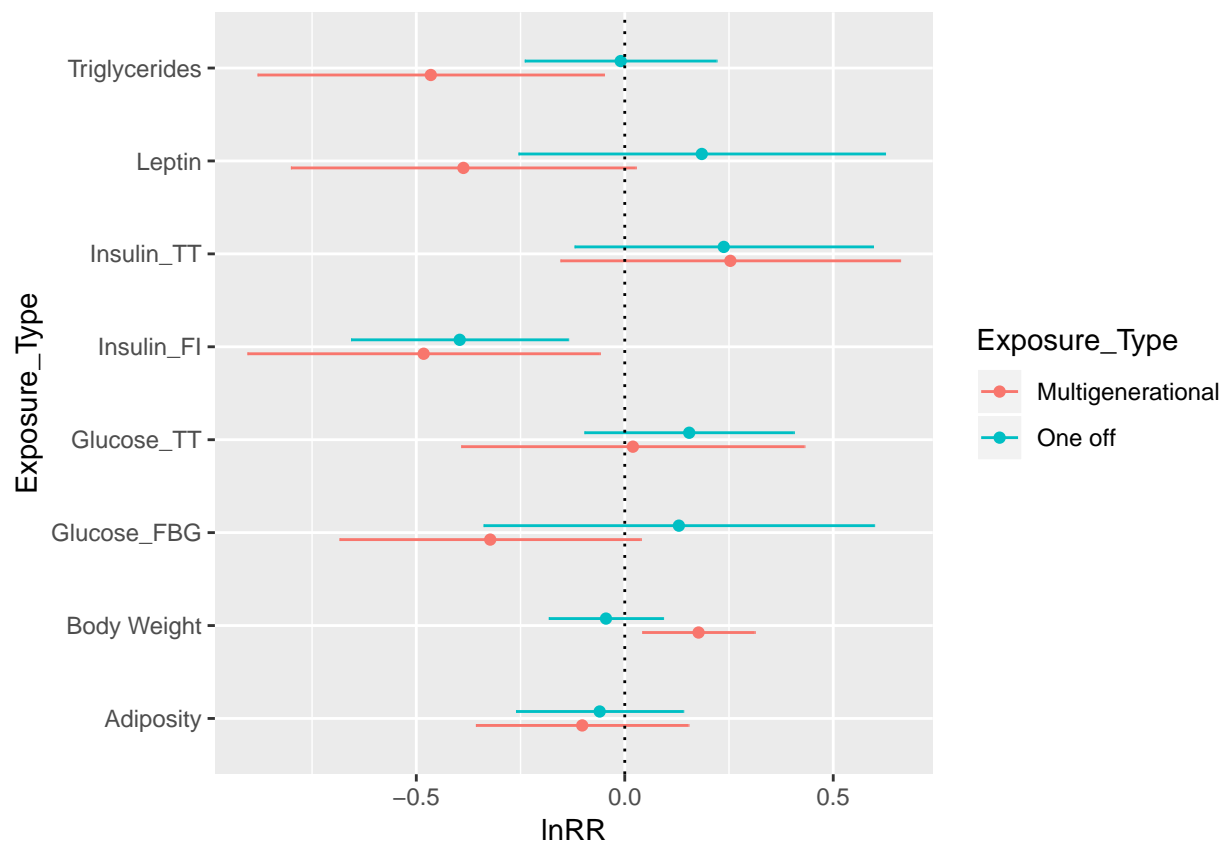

## Modelling all traits with moderators (split by exposure type)

```
All_Traits_Analysis_lnCVR_MG_f0 <- rma.mv(yi, vi, mods = ~F0_Parent_Exposed-1, random = list(~1|Trait,
```

```
## Warning in rma.mv(yi, vi, mods = ~F0_Parent_Exposed - 1, random = list(~1
## | : Redundant predictors dropped from the model.
```

```
summary(All_Traits_Analysis_lnCVR_MG_f0)
```

```
##
## Multivariate Meta-Analysis Model (k = 118; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -100.9803   201.9606   213.9606   230.4822   214.7313
##
## Variance Components:
##
##               estim    sqrt   nlvls   fixed     factor
## sigma^2.1    0.0498  0.2233       8      no      Trait
## sigma^2.2    0.0012  0.0352      13      no    Paper_ID
## sigma^2.3    0.0000  0.0001      24      no   Cohort_ID
## sigma^2.4    0.1518  0.3896     118      no       ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 116) = 324.9841, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:2):
## QM(df = 2) = 1.9988, p-val = 0.3681
##
## Model Results:
##
##                          estimate       se      zval      pval      ci.lb
## F0_Parent_ExposedFemale   -0.1175   0.1081   -1.0866   0.2772    -0.3294
## F0_Parent_ExposedMale     -0.1728   0.1285   -1.3444   0.1788    -0.4247
##                             ci.ub
## F0_Parent_ExposedFemale    0.0944
## F0_Parent_ExposedMale      0.0791
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
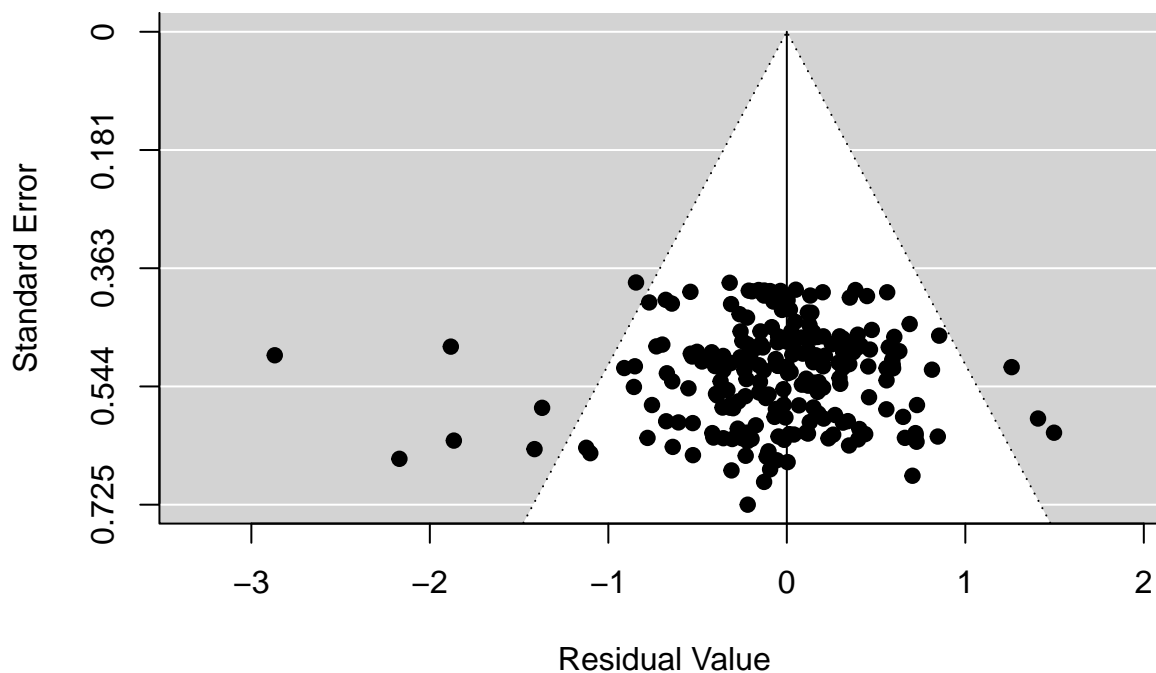
```
funnel(All_Traits_Analysis_lnCVR_MG_f0)
```
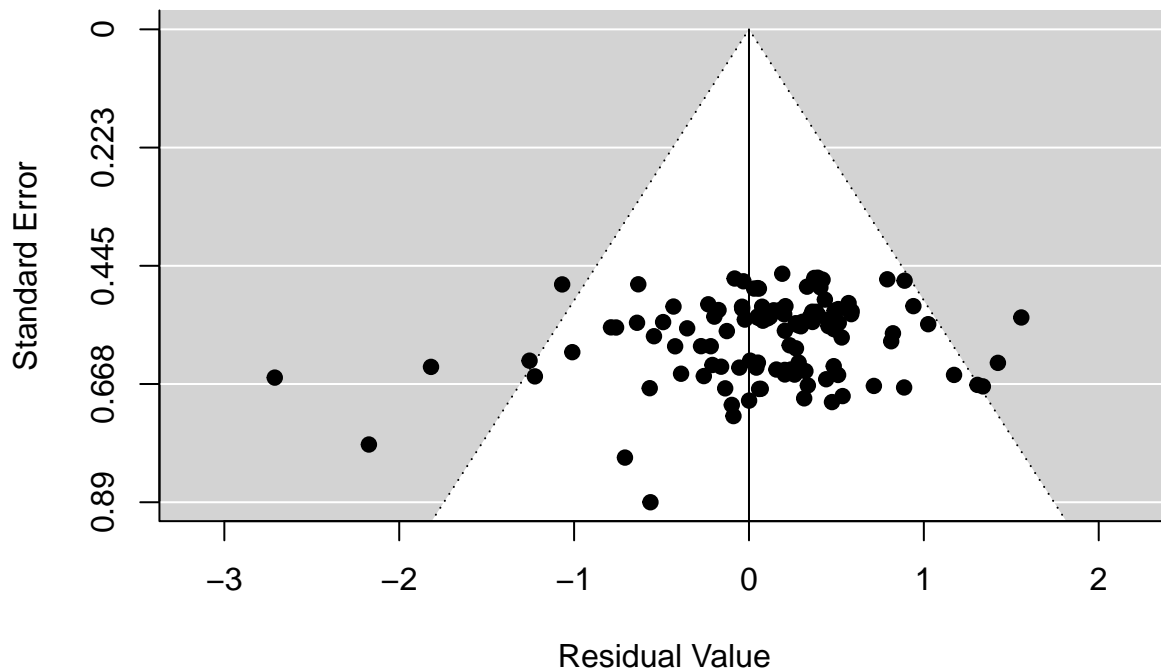
```r
All_Traits_Analysis_lnCVR_OF_f0 <- rma.mv(yi, vi, mods = ~F0_Parent_Exposed-1, random = list(~1|Trait,

summary(All_Traits_Analysis_lnCVR_OF_f0)
```

```
##
## Multivariate Meta-Analysis Model (k = 223; method: REML)
##
##     logLik   Deviance        AIC        BIC        AICc
## -160.1493   320.2985   334.2985   358.0539   334.8268
##
## Variance Components:
##
##              estim    sqrt  nlvls  fixed     factor
## sigma^2.1   0.0186  0.1363      8     no      Trait
## sigma^2.2   0.0345  0.1858     16     no   Paper_ID
## sigma^2.3   0.0031  0.0560     53     no  Cohort_ID
## sigma^2.4   0.0790  0.2810    223     no      ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 220) = 464.4483, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:3):
## QM(df = 3) = 0.0828, p-val = 0.9938
##
## Model Results:
```

```
##
##                         estimate      se     zval    pval    ci.lb
## F0_Parent_ExposedBoth    -0.0422  0.2543  -0.1658  0.8683  -0.5406
## F0_Parent_ExposedFemale  -0.0011  0.0915  -0.0122  0.9903  -0.1805
## F0_Parent_ExposedMale    -0.0336  0.1300  -0.2587  0.7959  -0.2884
##                            ci.ub
## F0_Parent_ExposedBoth     0.4562
## F0_Parent_ExposedFemale   0.1782
## F0_Parent_ExposedMale     0.2211
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```
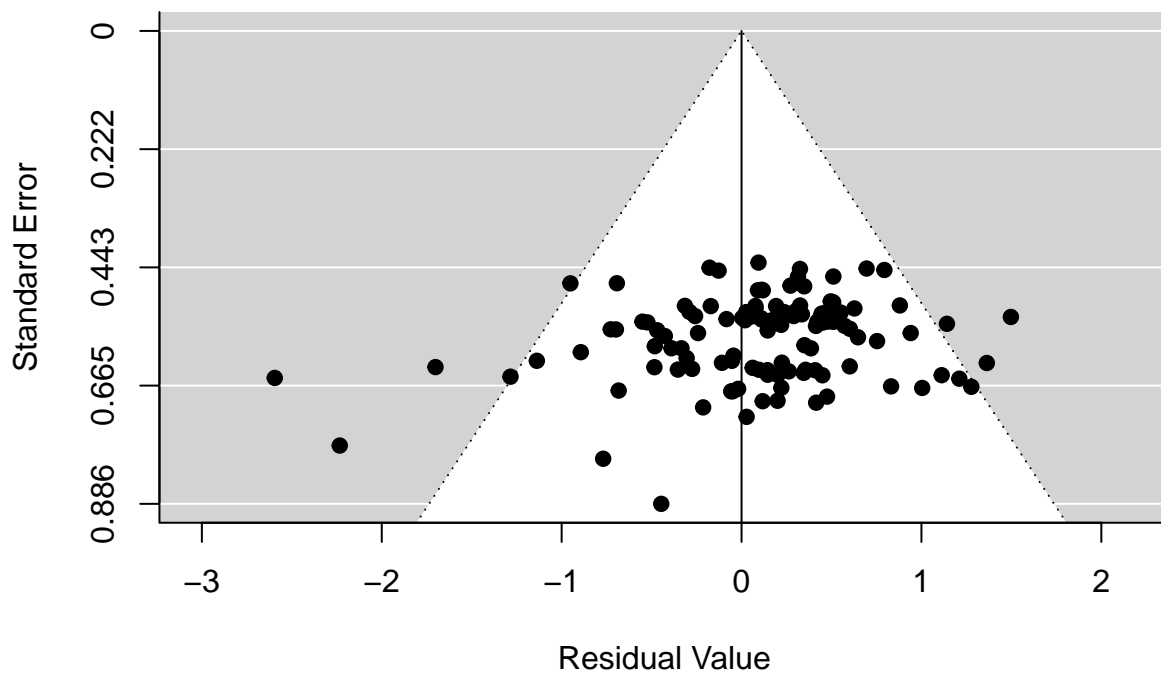
```r
funnel(All_Traits_Analysis_lnCVR_OF_f0)
```



```r
All_Traits_Analysis_lnCVR_MG_sex <- rma.mv(yi, vi, mods = ~Sex-1, random = list(~1|Trait, ~1|Paper_ID,~

summary(All_Traits_Analysis_lnCVR_MG_sex)
```

```
##
## Multivariate Meta-Analysis Model (k = 118; method: REML)
##
##   logLik  Deviance      AIC       BIC      AICc
## -99.1180  198.2360  212.2360  231.4505  213.2827
##
```

```
## Variance Components:
##
##            estim    sqrt  nlvls  fixed     factor
## sigma^2.1  0.0515  0.2269      8     no      Trait
## sigma^2.2  0.0000  0.0000     13     no   Paper_ID
## sigma^2.3  0.0000  0.0000     24     no  Cohort_ID
## sigma^2.4  0.1462  0.3824    118     no      ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 115) = 312.0097, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:3):
## QM(df = 3) = 5.2684, p-val = 0.1532
##
## Model Results:
##
##            estimate      se     zval    pval    ci.lb    ci.ub
## SexBoth     -0.0216  0.1719  -0.1257  0.8999  -0.3585   0.3153
## SexFemale   -0.0574  0.1151  -0.4988  0.6179  -0.2830   0.1682
## SexMale     -0.2344  0.1149  -2.0403  0.0413  -0.4596  -0.0092  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_lnCVR_MG_sex)
```

```
All_Traits_Analysis_lnCVR_OF_sex <- rma.mv(yi, vi, mods = ~Sex-1, random = list(~1|Trait, ~1|Paper_ID,~1

summary(All_Traits_Analysis_lnCVR_OF_sex)
```

```
##
## Multivariate Meta-Analysis Model (k = 223; method: REML)
##
##     logLik   Deviance        AIC        BIC       AICc
## -160.0026   320.0052   334.0052   357.7606   334.5335
##
## Variance Components:
##
##              estim    sqrt  nlvls  fixed    factor
## sigma^2.1   0.0215  0.1466      8     no     Trait
## sigma^2.2   0.0324  0.1800     16     no   Paper_ID
## sigma^2.3   0.0036  0.0602     53     no  Cohort_ID
## sigma^2.4   0.0779  0.2791    223     no     ES_ID
##
## Test for Residual Heterogeneity:
## QE(df = 220) = 463.8208, p-val < .0001
##
## Test of Moderators (coefficient(s) 1:3):
## QM(df = 3) = 0.8385, p-val = 0.8402
##
## Model Results:
##
##             estimate       se     zval     pval    ci.lb   ci.ub
## SexBoth      -0.3733   0.4110  -0.9081   0.3638  -1.1789  0.4323
## SexFemale     0.0043   0.0939   0.0462   0.9631  -0.1796  0.1883
## SexMale      -0.0002   0.0931  -0.0019   0.9985  -0.1827  0.1823
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(All_Traits_Analysis_lnCVR_OF_sex)
```
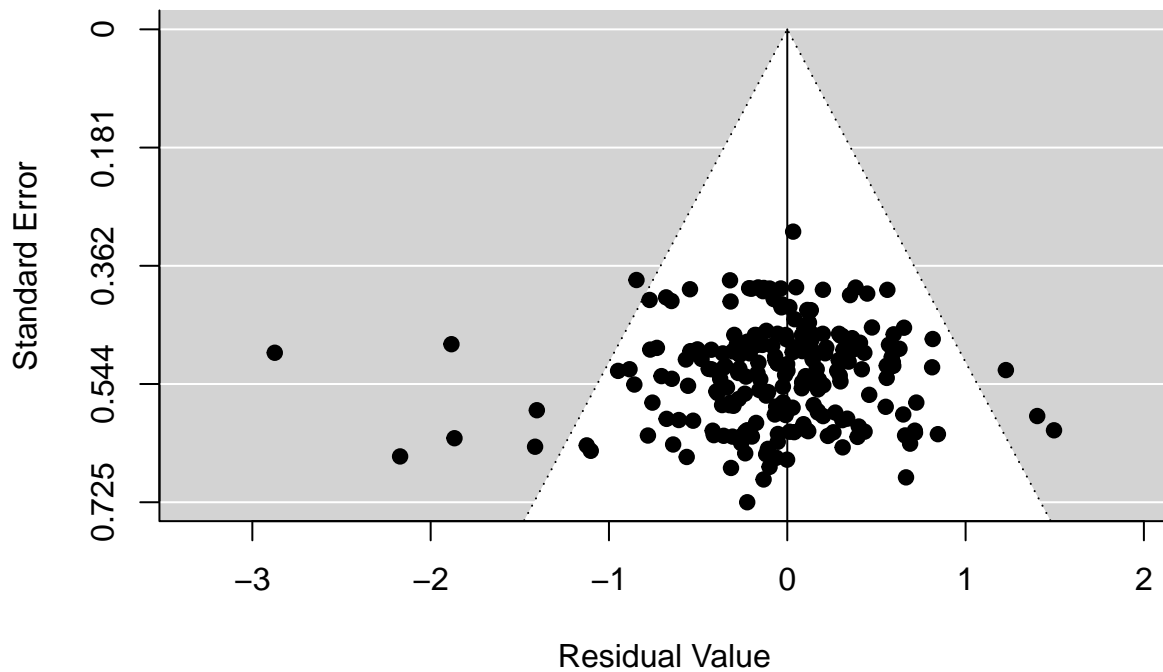
```
Overall_Exp_mods_lnCVR <- tibble(
  Exposure_Type = c("Multigenerational","Multigenerational", "One off", "One off", "One off", "Multigen
  mod = c("F0 Female","F0 Male", "F0 Both", "F0 Female", "F0 Male","Both Offspring Sex","Female Offsprin
  lnCVR = c(-0.1175,-0.1728,-0.0418,-0.0011,-0.0329,-0.0204,-0.0522,-0.2292,-0.3737,-0.0034,0.0073),
  ci.lb = c(-0.3294,-0.4247,-0.5383,-0.1806,-0.2872,-0.3612,-0.2875,-0.4567,-1.1772,-0.1879,-0.1742),
  ci.ub = c(0.0944,0.0791,0.4547,0.1784,0.2215,0.3205,0.1832,-0.0017,0.4298,0.1812,0.1889)
)

plot_lnCVR_overall_mods_exp <- ggplot(Overall_Exp_mods_lnCVR, aes(x=mod, y=lnCVR, colour=Exposure_Type))
  geom_errorbar(aes(ymin=ci.lb, ymax=ci.ub), width = 0, position = position_dodge(0.3)) +
  geom_point(aes(x = mod, y = lnCVR), position = position_dodge(0.3))+
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "mod", y = "lnCVR") +
  coord_flip()

plot_lnCVR_overall_mods_exp
```