

Leptin

Meta-regression Insulin

```
load(file="Effect_Size_All_Traits.RData")
load(file="Effect_Size_All_Traits_lnCVR.RData")

Leptin_lnRR <- subset(Effect_Size_All_Traits, Effect_Size_All_Traits$Trait == "Leptin")
Leptin_lnCVR <- subset(Effect_Size_All_Traits_lnCVR, Effect_Size_All_Traits_lnCVR$Trait == "Leptin")

Leptin_lnRR_MG <- subset(Leptin_lnRR, Leptin_lnRR$Exposure_Type == "Multigenerational")
Leptin_lnRR_OF <- subset(Leptin_lnRR, Leptin_lnRR$Exposure_Type == "One off")

Leptin_lnCVR_MG <- subset(Leptin_lnCVR, Leptin_lnCVR$Exposure_Type == "Multigenerational")
Leptin_lnCVR_OF <- subset(Leptin_lnCVR, Leptin_lnCVR$Exposure_Type == "One off")
```

Overall analysis

```
Leptin_overall_lnRR_0mods <- rma.mv(yi, vi, random = list(~1|ES_ID, ~1|Cohort_ID), data=Leptin_lnRR, method="REML")
#Random factors account for no independence and Cohort ID is more biologically meaningful. Can use only
summary(Leptin_overall_lnRR_0mods)
```

```
##
## Multivariate Meta-Analysis Model (k = 12; method: REML)
##
##   logLik  Deviance      AIC      BIC      AICc
## -14.2064   28.4128   34.4128   35.6065   37.8414
##
## Variance Components:
##
##           estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.0190  0.1377     12     no      ES_ID
## sigma^2.2  2.5210  1.5878      8     no  Cohort_ID
##
## Test for Heterogeneity:
## Q(df = 11) = 209.8993, p-val < .0001
##
## Model Results:
##
## estimate      se    zval    pval   ci.lb   ci.ub
##   1.1962   0.5691  2.1020  0.0356  0.0808  2.3115  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
#Tibble of overall results
```

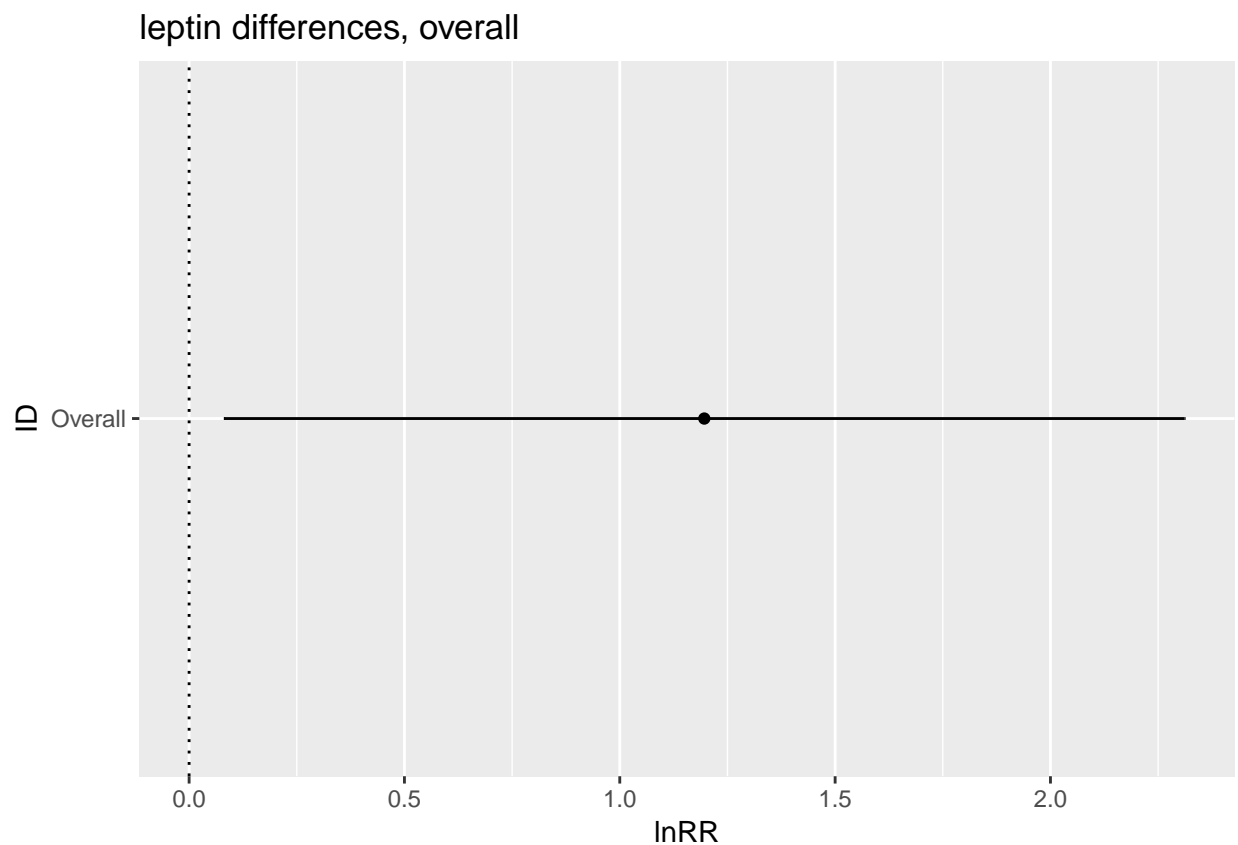
```
Leptin_overall_lnRR <- tibble(  
  ID = "Overall",  
  lnRR = 1.1962,  
  ci.lb = 0.0808,  
  ci.ub = 2.3115  
)
```

```
## Warning: `list_len()` is deprecated as of rlang 0.2.0.
```

```
## Please use `new_list()` instead.
```

```
## This warning is displayed once per session.
```

```
plot_leptin_overall <- ggplot(Leptin_overall_lnRR, 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(title = "leptin differences, overall", x = "ID", y = "lnRR") +  
  coord_flip()  
plot_leptin_overall
```

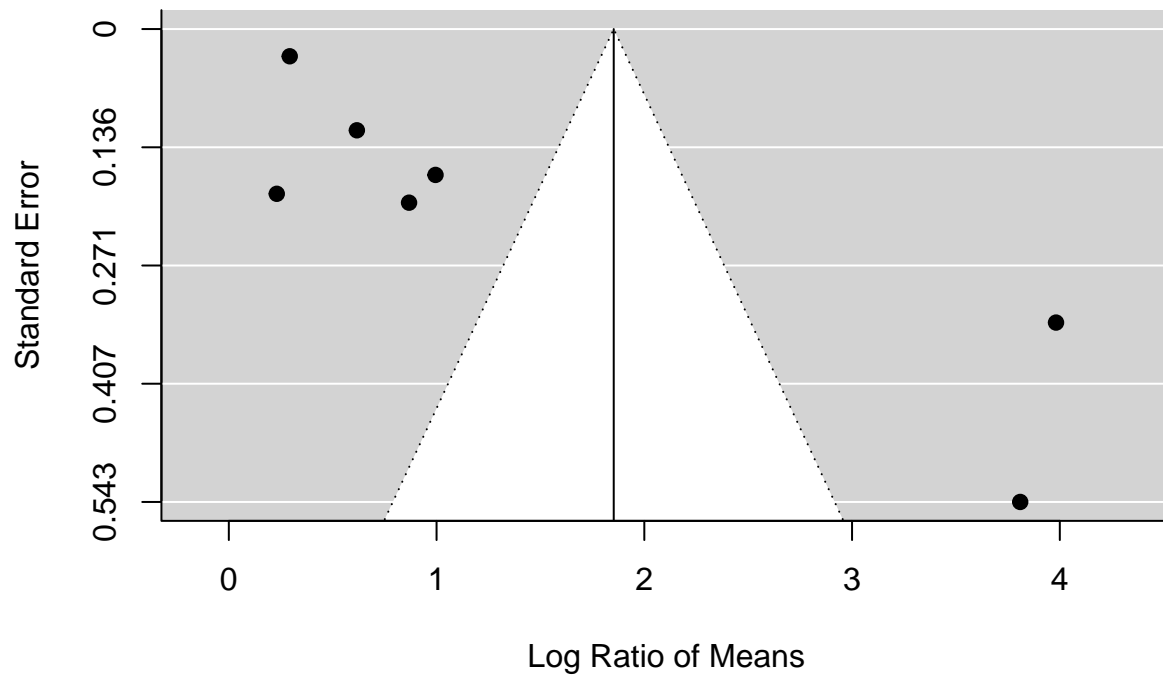


```
#Analysis split by exposure type
```

```
Leptin_lnRR_MG <- rma.mv(yi, vi, random = list(~1|ES_ID, ~1|Cohort_ID), data=Leptin_lnRR_MG, method = 'REML')  
summary(Leptin_lnRR_MG)
```

```
##
## Multivariate Meta-Analysis Model (k = 7; method: REML)
##
##   logLik  Deviance      AIC      BIC      AICc
## -8.3474   16.6948   22.6948   22.0701   34.6948
##
## Variance Components:
##
##           estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.0182  0.1350      7     no      ES_ID
## sigma^2.2  3.2130  1.7925      5     no  Cohort_ID
##
## Test for Heterogeneity:
## Q(df = 6) = 186.3769, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
##   1.8529  0.8138  2.2769  0.0228  0.2579  3.4478  *
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

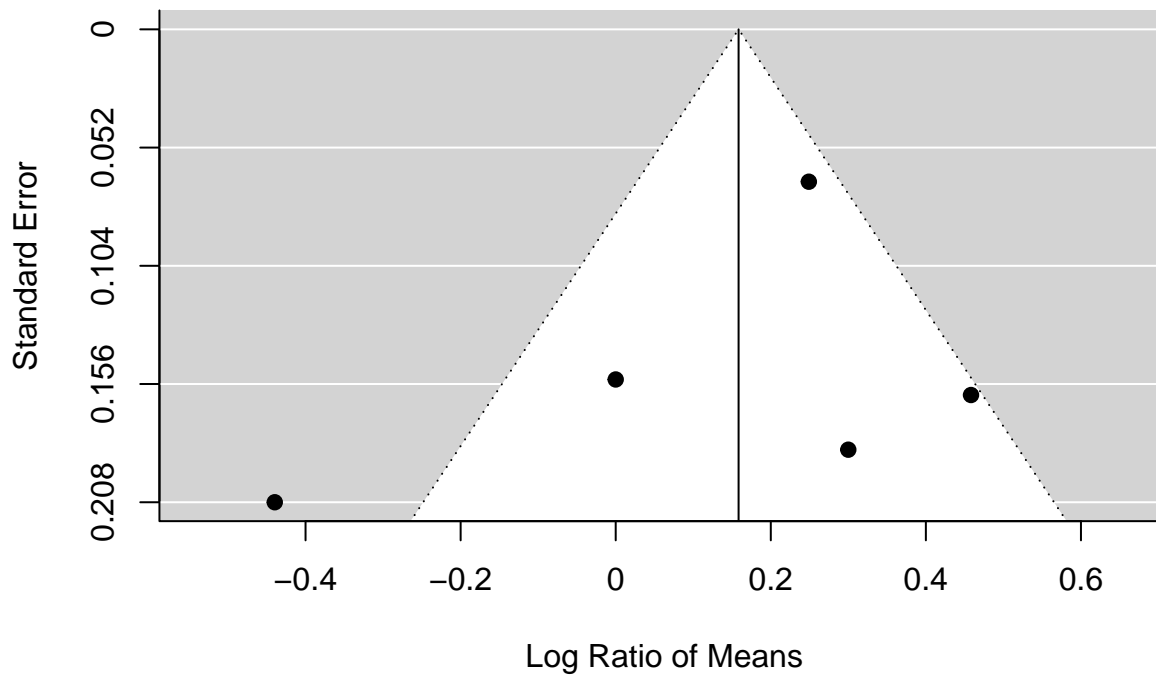
```
funnel(Leptin_lnRR_MG)
```



```
Leptin_lnRR_OF <- rma.mv(yi, vi, random = list(~1|ES_ID,~1|Cohort_ID), data=Leptin_lnRR_OF, method = 'REML')
summary(Leptin_lnRR_OF)
```

```
##
## Multivariate Meta-Analysis Model (k = 5; method: REML)
##
##   logLik  Deviance      AIC      BIC      AICc
## -0.7120   1.4240   7.4240   5.5829   31.4240
##
## Variance Components:
##
##           estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.0100  0.0999     5     no      ES_ID
## sigma^2.2  0.0626  0.2502     3     no  Cohort_ID
##
## Test for Heterogeneity:
## Q(df = 4) = 14.6126, p-val = 0.0056
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
##  0.1585  0.1641  0.9660  0.3341  -0.1631  0.4801
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(Leptin_lnRR_OF)
```



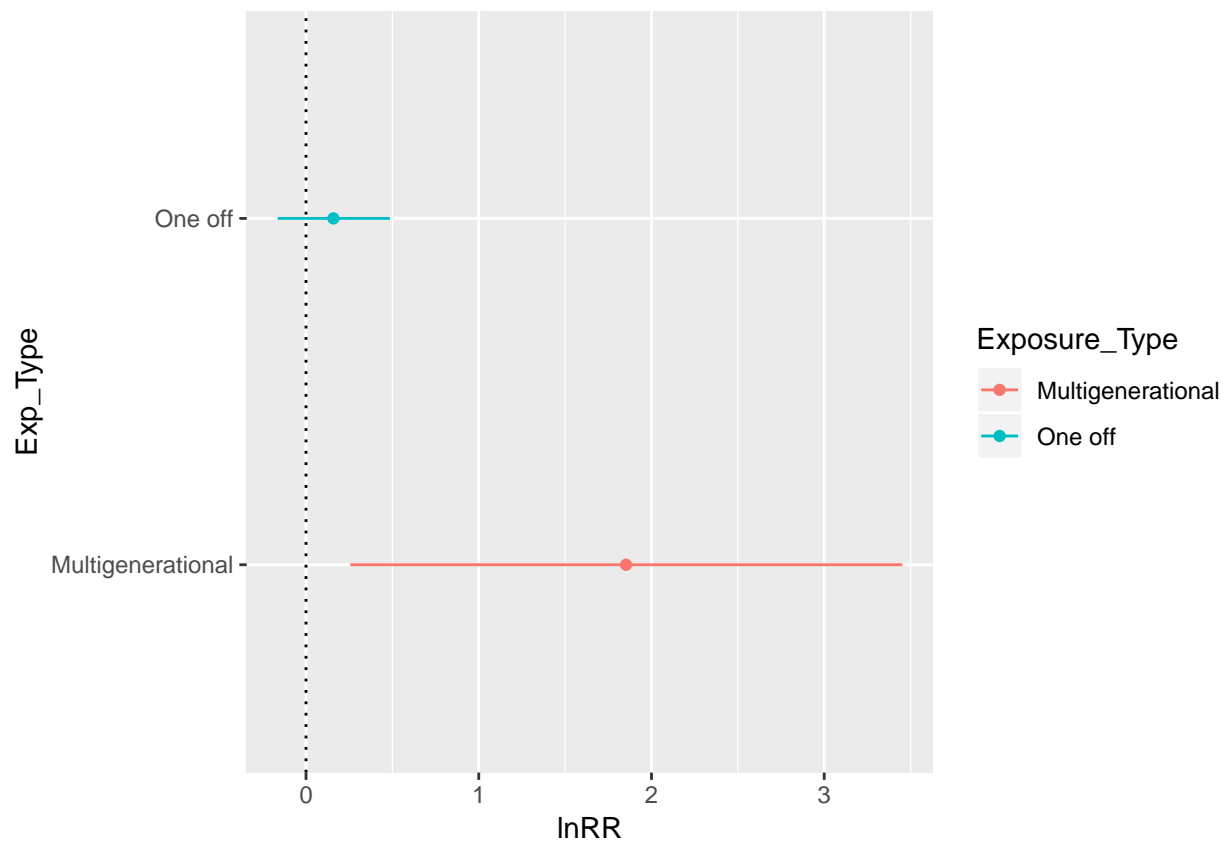
```
Leptin_Exp_lnRR <- tibble(
  Exposure_Type = c("Multigenerational", "One off"),
  lnRR = c(1.8529, 0.1585),
  ci.lb = c(0.2579, -0.1631),
  ci.ub = c(3.4478, 0.4801)
)
```

```
Leptin_Exp_lnRR
```

```
## # A tibble: 2 x 4
##   Exposure_Type    lnRR  ci.lb ci.ub
##   <chr>          <dbl> <dbl> <dbl>
## 1 Multigenerational 1.85   0.258 3.45
## 2 One off          0.158 -0.163 0.480
```

```
#Plotting when split by exp type
```

```
plot_Leptin_exp_type <- ggplot(Leptin_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 = "Exp_Type", y = "lnRR") +
  coord_flip()
plot_Leptin_exp_type
```



Leptin lnCVR analysis

```
Leptin_overall_lnCVR_0mods <- rma.mv(yi, vi, random = list(~1|ES_ID, ~1|Cohort_ID), data=Leptin_lnCVR, method="REML")
#Random factors account for no independence and Cohort ID is more biologically meaningful. Can use only ES_ID
summary(Leptin_overall_lnCVR_0mods)
```

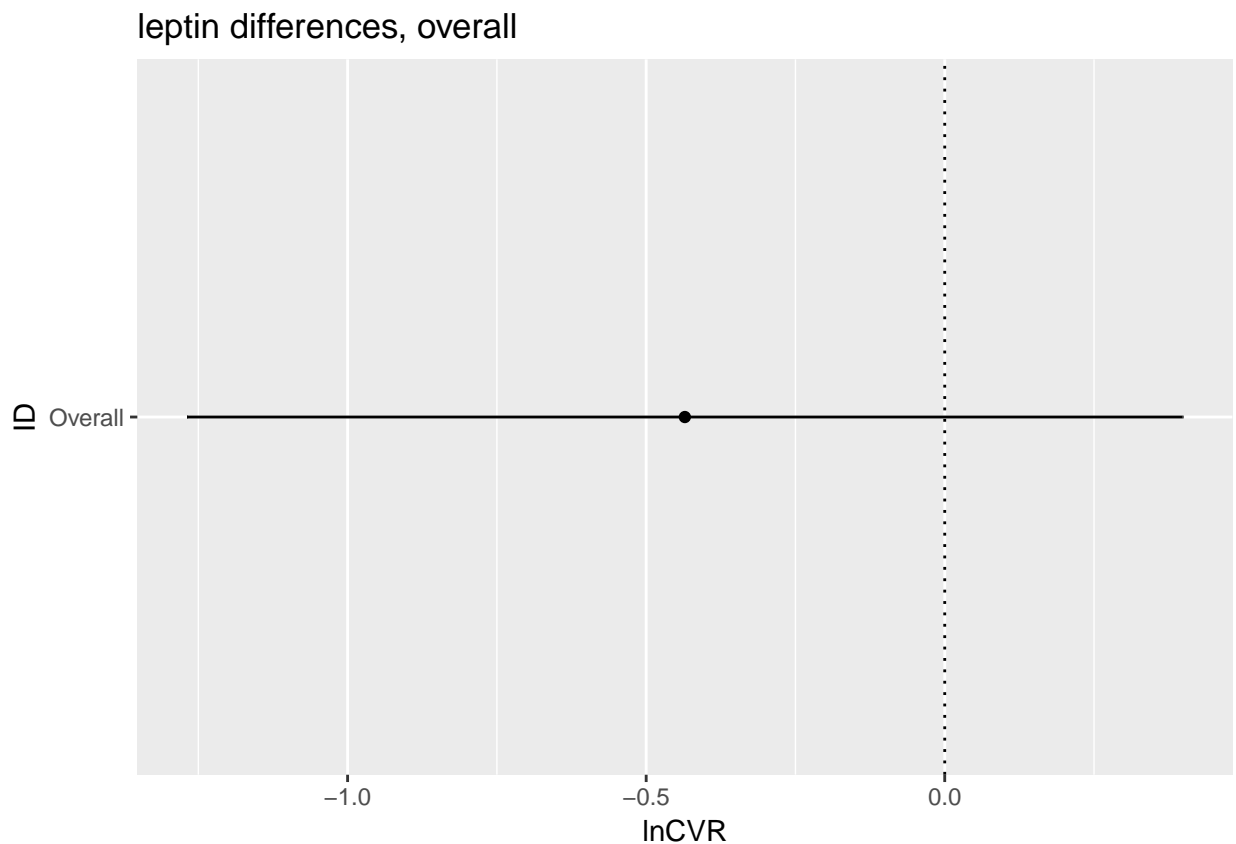
```
##
## Multivariate Meta-Analysis Model (k = 12; method: REML)
##
##   logLik  Deviance      AIC      BIC      AICc
## -13.3225  26.6450  32.6450  33.8387  36.0736
##
## Variance Components:
##
##      estim  sqrt  nlvls  fixed  factor
## sigma^2.1  0.0000  0.0000   12    no    ES_ID
## sigma^2.2  1.2997  1.1400    8    no  Cohort_ID
##
## Test for Heterogeneity:
## Q(df = 11) = 53.2636, p-val < .0001
##
```

```
## Model Results:
##
## estimate      se      zval    pval    ci.lb    ci.ub
## -0.4352  0.4253  -1.0233  0.3062  -1.2688  0.3984
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

#Tibble of overall results

```
Leptin_overall_lnCVR <- tibble(
  ID = "Overall",
  lnCVR = -0.4352,
  ci.lb = -1.2688,
  ci.ub = 0.3984
)

plot_leptin_overall_lnCVR <- ggplot(Leptin_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(title = "leptin differences, overall", x = "ID", y = "lnCVR") +
  coord_flip()
plot_leptin_overall_lnCVR
```

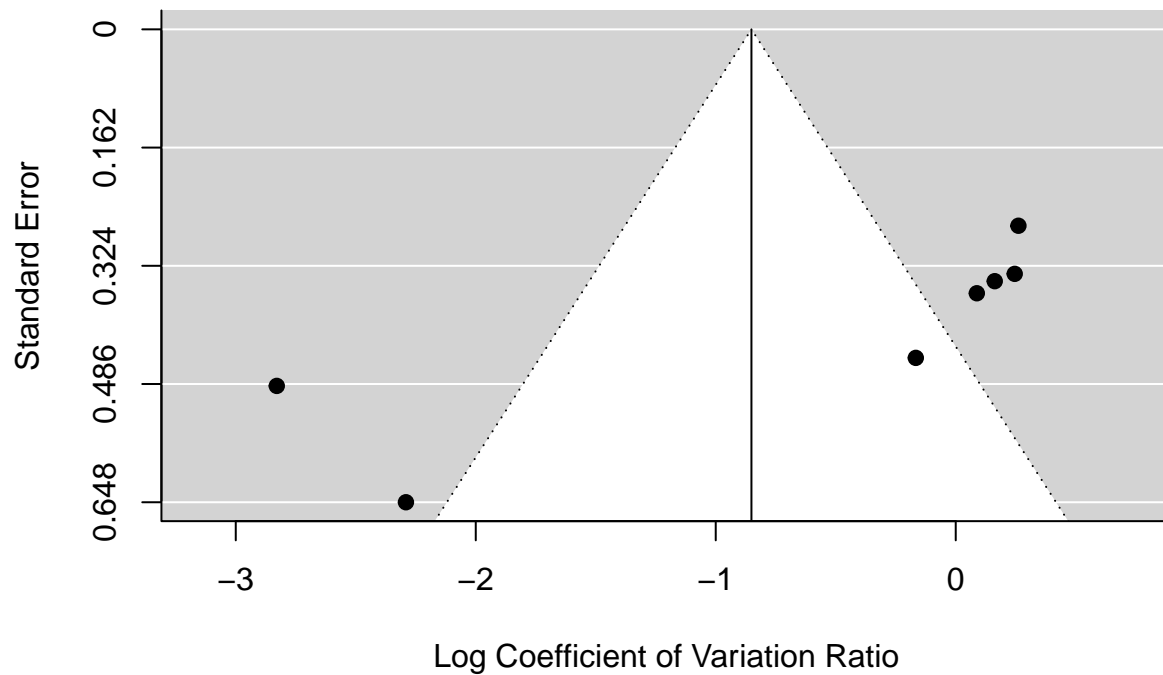


#Analysis split by exposure type

```
Leptin_lnCVR_MG <- rma.mv(yi, vi, random = list(~1|ES_ID, ~1|Cohort_ID), data=Leptin_lnCVR_MG, method =
summary(Leptin_lnCVR_MG)
```

```
##
## Multivariate Meta-Analysis Model (k = 7; method: REML)
##
##   logLik  Deviance      AIC      BIC      AICc
##   -7.9645   15.9290   21.9290   21.3043   33.9290
##
## Variance Components:
##
##           estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.0000  0.0000     7     no      ES_ID
## sigma^2.2  2.0294  1.4246     5     no  Cohort_ID
##
## Test for Heterogeneity:
## Q(df = 6) = 45.8830, p-val < .0001
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
##   -0.8512   0.6631  -1.2838   0.1992   -2.1508   0.4483
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

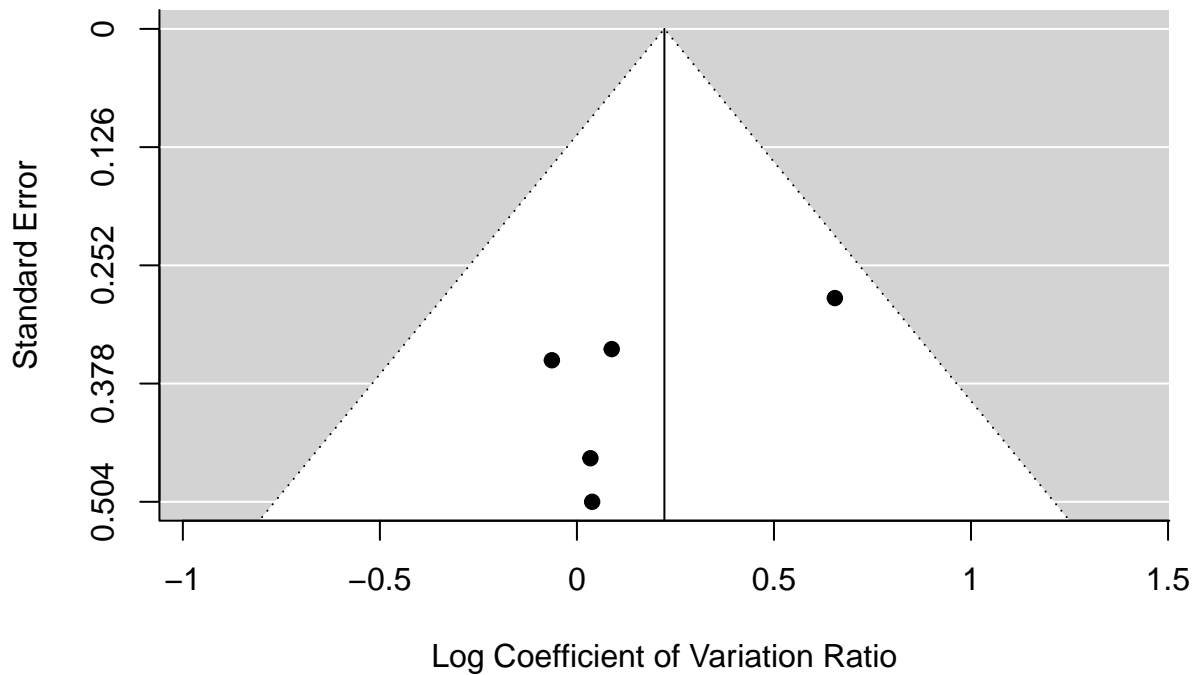
```
funnel(Leptin_lnCVR_MG)
```

```
Leptin_lnCVR_OF <- rma.mv(yi, vi, random = list(~1|ES_ID, ~1|Cohort_ID), data=Leptin_lnCVR_OF, method =
summary(Leptin_lnCVR_OF)
```

```
##
## Multivariate Meta-Analysis Model (k = 5; method: REML)
##
##   logLik  Deviance      AIC      BIC      AICc
## -1.5021    3.0042    9.0042    7.1631    33.0042
##
## Variance Components:
##
##           estim      sqrt  nlvls  fixed      factor
## sigma^2.1  0.0000  0.0000     5    no      ES_ID
## sigma^2.2  0.0214  0.1464     3    no    Cohort_ID
##
## Test for Heterogeneity:
## Q(df = 4) = 3.3745, p-val = 0.4972
##
## Model Results:
##
## estimate      se      zval      pval      ci.lb      ci.ub
##  0.2219  0.1881  1.1797  0.2381  -0.1468  0.5906
##
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
funnel(Leptin_lnCVR_OF)
```



```
Leptin_Exp_lnCVR <- tibble(
  Exposure_Type = c("Multigenerational", "One off"),
  lnCVR = c(-0.8512, 0.2219),
  ci.lb = c(-2.1508, -0.1468),
  ci.ub = c(0.4483, 0.5906)
)
```

```
Leptin_Exp_lnCVR
```

```
## # A tibble: 2 x 4
##   Exposure_Type    lnCVR  ci.lb ci.ub
##   <chr>          <dbl> <dbl> <dbl>
## 1 Multigenerational -0.851 -2.15  0.448
## 2 One off           0.222 -0.147 0.591
```

```
#Plotting when split by exp type
```

```
plot_Leptin_exp_type_lnCVR <- ggplot(Leptin_Exp_lnCVR, aes(x=Exposure_Type, 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 = Exposure_Type, y = lnCVR), position = position_dodge(0.3)) +
  geom_hline(yintercept = 0, lty = "dotted") +
  labs(x = "Exp_Type", y = "lnCVR") +
```

```
coord_flip()  
plot_Leptin_exp_type_lnCVR
```

