

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

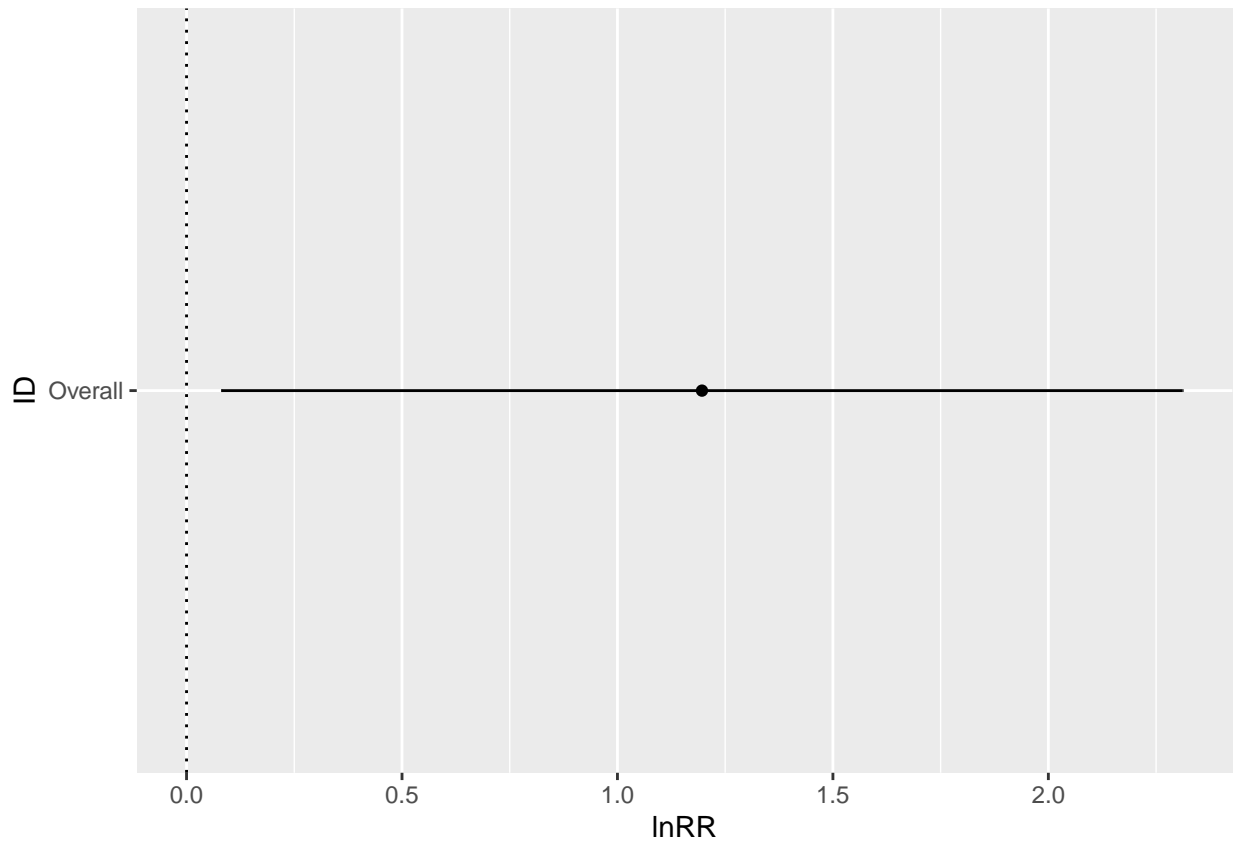
```
Leptin_overall_lnRR_0mods <- rma.mv(yi, vi, random = list(~1|ES_ID, ~1|Cohort_ID), data=Leptin_lnRR, method="REML")
#Random factors account for no independence and Cohort ID is more biologically meaningful. Can use only ES_ID
summary(Leptin_overall_lnRR_0mods)
```

```
##
## 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 = Leptin_overall_lnRR_Omods$b[1],
  ci.lb = Leptin_overall_lnRR_Omods$ci.lb[1],
  ci.ub = Leptin_overall_lnRR_Omods$ci.ub[1]
)

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(x = "ID", y = "lnRR") +
  coord_flip()
plot_leptin_overall
```



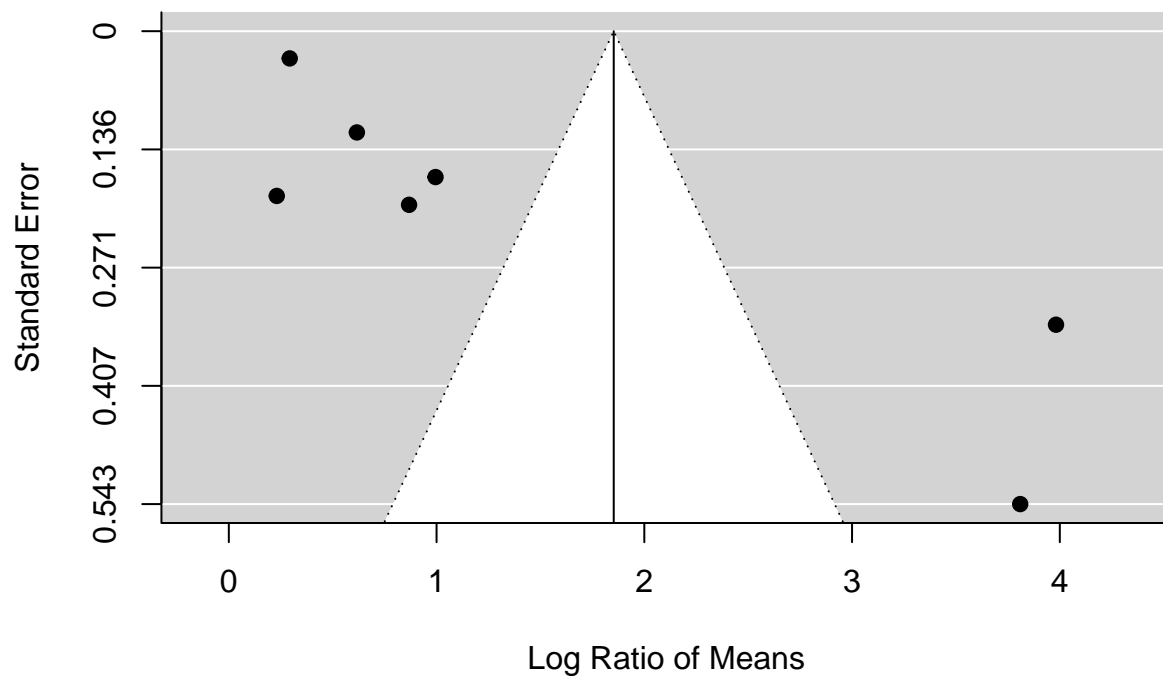
```
#Analysis split by exposure type
```

```
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
```

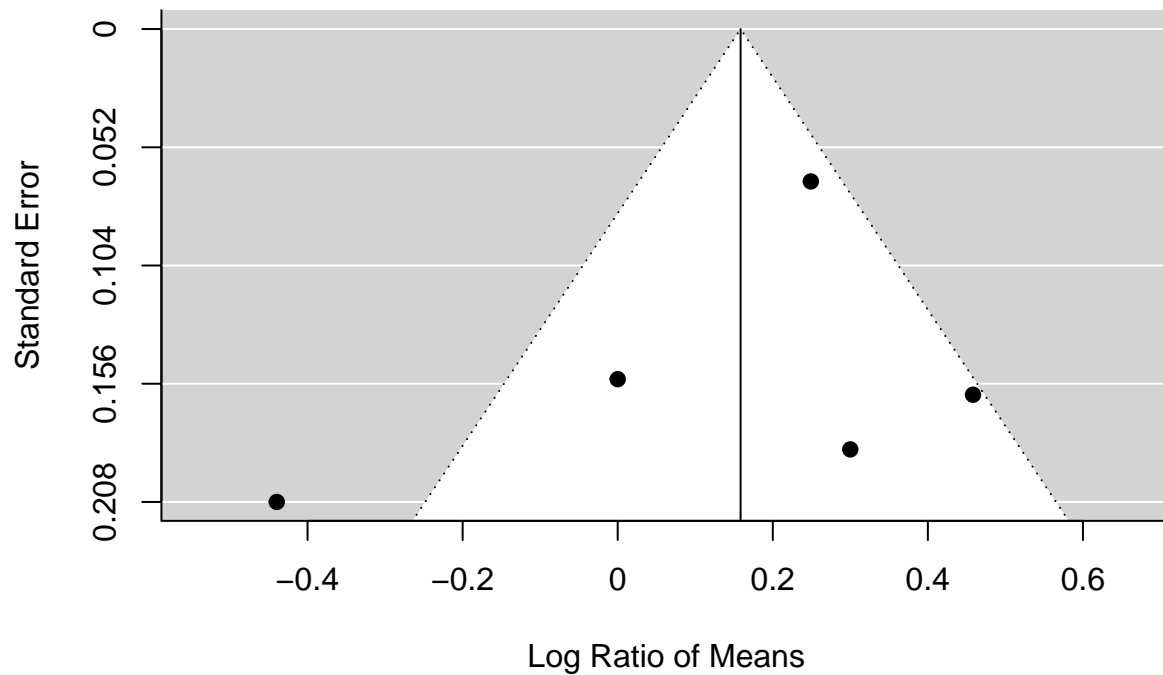
```
funnel(Leptin_lnRR_MG)
```



```
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)
```



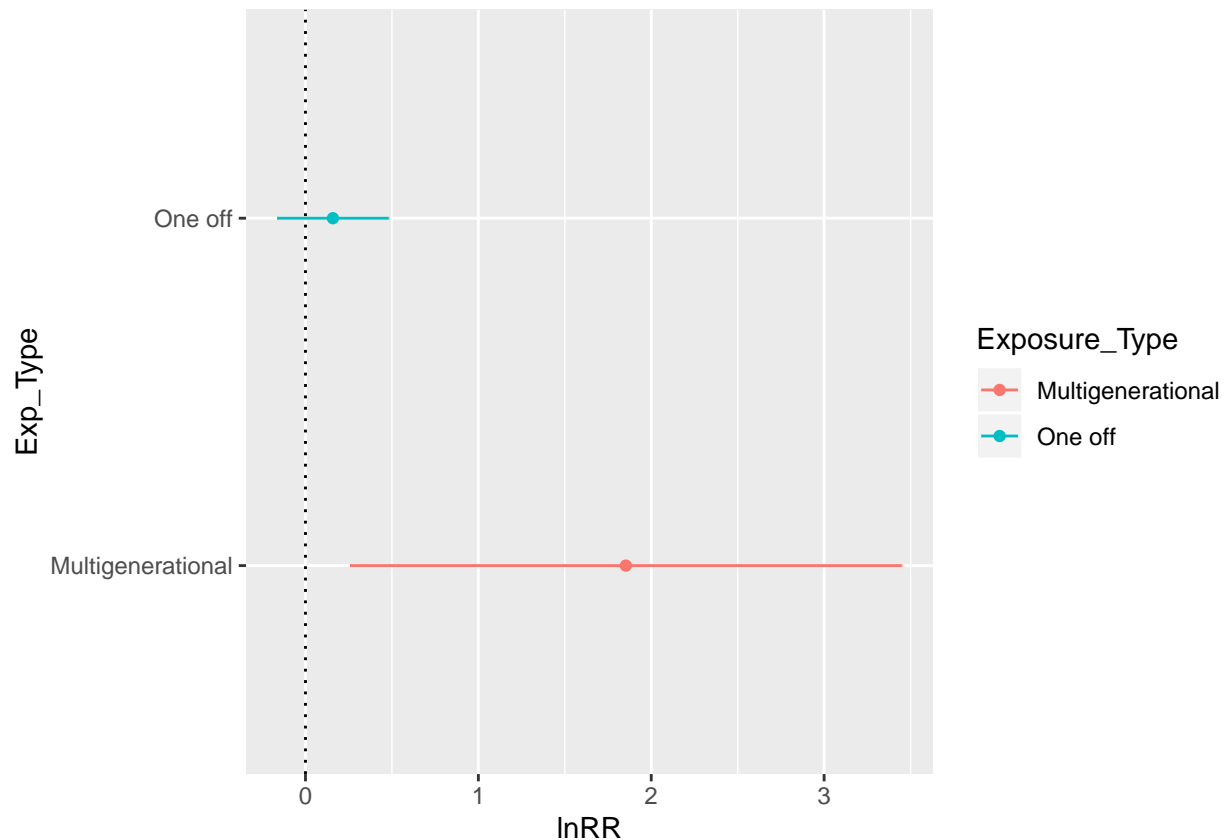
```
Leptin_Exp_lnRR <- tibble(
  Exposure_Type = c("Multigenerational", "One off"),
  lnRR = c(Leptin_lnRR_MG$b[1], Leptin_lnRR_OF$b[1]),
  ci.lb = c(Leptin_lnRR_MG$ci.lb[1], Leptin_lnRR_OF$ci.lb[1]),
  ci.ub = c(Leptin_lnRR_MG$ci.ub[1], Leptin_lnRR_OF$ci.ub[1])
)
```

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
```



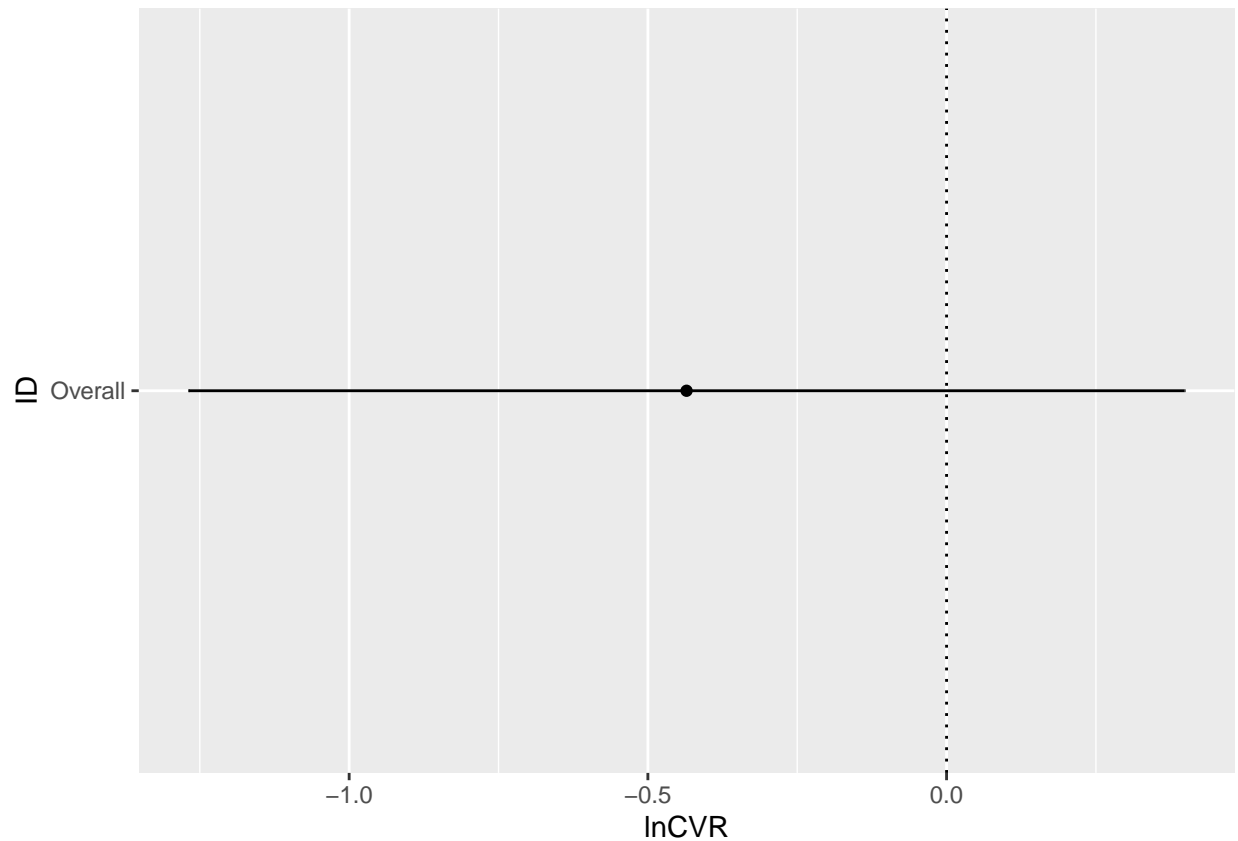
Leptin lnCVR analysis

```
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  
  
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 = Leptin_overall_lnCVR_0mods$b[1],  
  ci.lb = Leptin_overall_lnCVR_0mods$ci.lb[1],  
  ci.ub = Leptin_overall_lnCVR_0mods$ci.ub[1]  
)  
  
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(x = "ID", y = "lnCVR") +  
  coord_flip()  
plot_leptin_overall_lnCVR
```



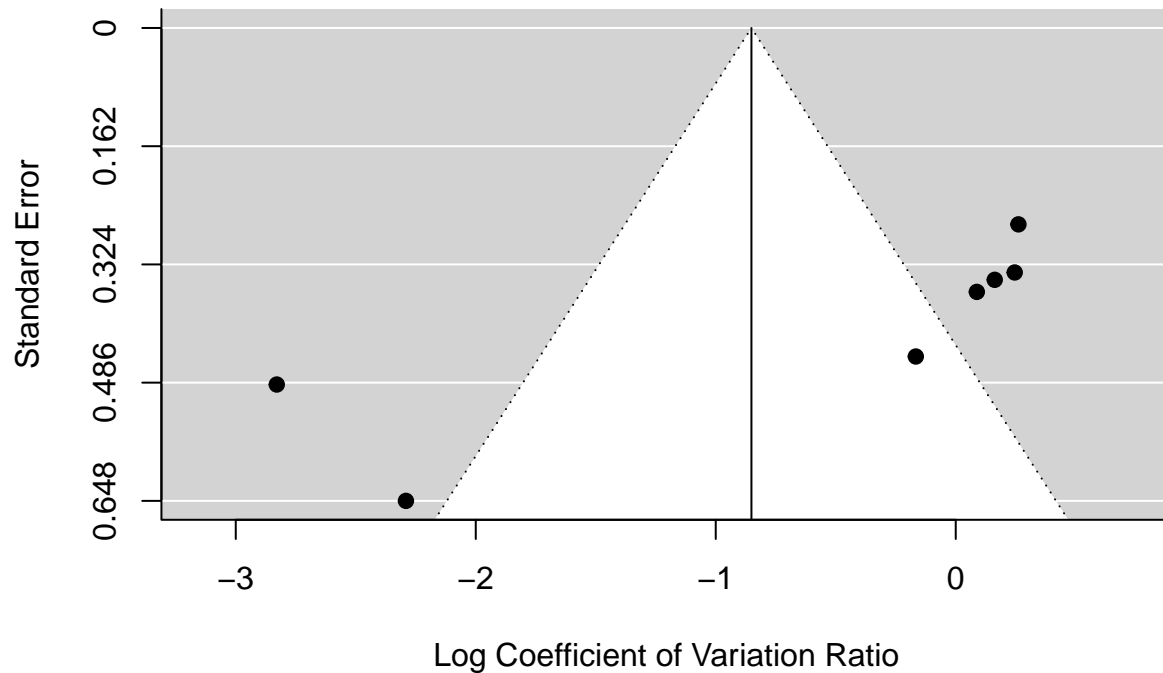
#Analysis split by exposure type

```
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)
```



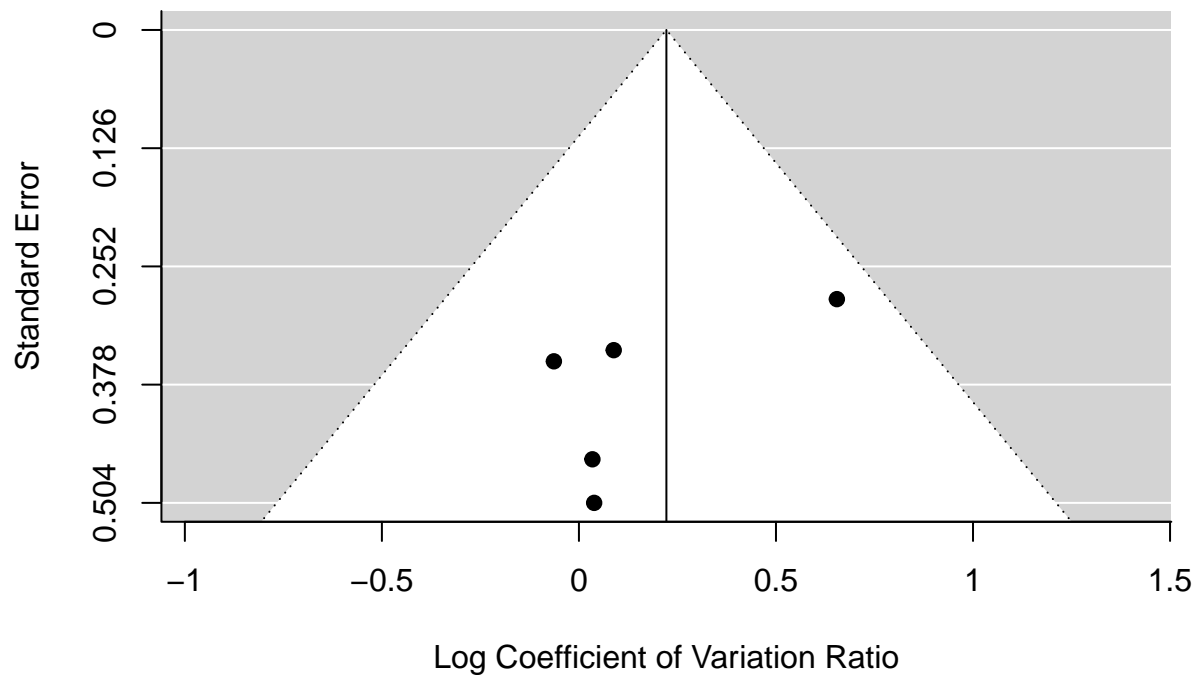
```
Leptin_lnCVR_OF <- rma.mv(yi, vi, random = list(~1|ES_ID,~1|Cohort_ID), data=Leptin_lnCVR_OF, method =
summary(Leptin_lnCVR_OF)
```

```
##
## 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(Leptin_lnCVR_MG$b[1], Leptin_lnCVR_OF$b[1]),
  ci.lb = c(Leptin_lnCVR_MG$ci.lb[1], Leptin_lnCVR_OF$ci.lb[1]),
  ci.ub = c(Leptin_lnCVR_MG$ci.ub[1], Leptin_lnCVR_OF$ci.ub[1])
)
```

```
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
```

