Prenatal and childhood exposure to per-/polyfluoroalkyl substances (PFASs) and its associations with childhood overweight and/or obesity: a systematic review with meta-analyses

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**Supplementary text**

**Text string used for the search in PubMed:**

(((("Pediatric Obesity"[Mesh]) OR ("Obesity"[Mesh] AND (allchild[Filter] OR "Breast Feeding"[Mesh])) OR ("Overweight"[Mesh] AND (allchild[Filter] OR "Breast Feeding"[Mesh])) OR ("Overnutrition"[Mesh] AND (allchild[Filter] OR "Breast Feeding"[Mesh]))) AND (("Fluorocarbons"[Mesh]) OR ("Hydrocarbons, Fluorinated "[MESH]) OR ("Fluorocarbon Polymers "[MESH]) OR ("perfluoropentanoic acid" [Supplementary Concept]) OR ("perfluorododecanoic acid" [Supplementary Concept]) OR ("perfluorohexanesulfonic acid" [Supplementary Concept]) OR ("2-((6-chloro-1,1,2,2,3,3,4,4,5,5,6,6-dodecafluorohexyl)oxy)-1,1,2,2-tetrafluoroethanesulfonic acid" [Supplementary Concept]))) OR ((newborn\*[Title/Abstract] OR neonat\*[Title/Abstract] OR infan\*[Title/Abstract] OR toddler\*[Title/Abstract] OR kid[Title/Abstract] OR kids[Title/Abstract] OR baby[Title/Abstract] OR babies[Title/Abstract] OR boy[Title/Abstract] OR boys[Title/Abstract] OR girl\*[Title/Abstract] OR child\*[Title/Abstract] OR adolescen\*[Title/Abstract] OR teen\*[Title/Abstract] OR pediatr\*[Title/Abstract] OR paediatr\*[Title/Abstract] OR prenat\*[Title/Abstract] OR intrauter\*[Title/Abstract] OR pregnant\*[Title/Abstract] OR gestat\*[Title/Abstract] OR gravid\*[Title/Abstract] OR fetus[Title/Abstract] OR breastfeed\*[Title/Abstract] OR nourish[Title/Abstract] OR nursing[Title/Abstract] OR suckling[Title/Abstract] OR lactate[Title/Abstract] OR milk[Title/Abstract]) AND ((Obes\*[Title/Abstract]) OR (Overweight\*[Title/Abstract]) OR (Overnutrition[Title/Abstract]) OR (BMI[Title/Abstract]) OR (“body mass index”[Title/Abstract]) OR (weight[Title/Abstract]) OR (height[Title/Abstract]) OR (“waist circumference”[Title/Abstract]) OR (WC[Title/Abstract]) OR (“fat mass”[Title/Abstract]) OR (FM[Title/Abstract]) OR (“body fat”[Title/Abstract]) OR (adipos\*[Title/Abstract])) AND ((Fluorocarb\*[Title/Abstract]) OR (polyfluoro\*[Title/Abstract]) OR (perfluoro\*[Title/Abstract]) OR (PFAS[Title/Abstract]) OR (PFBA[Title/Abstract]) OR (PFPeA[Title/Abstract]) OR (PFHxA[Title/Abstract]) OR (PFHpA[Title/Abstract]) OR (PFOA[Title/Abstract]) OR (PFNA[Title/Abstract]) OR (PFDA[Title/Abstract]) OR (PFUnDA[Title/Abstract]) OR (PFDoDA[Title/Abstract]) OR (PFTrDA[Title/Abstract]) OR (PFTeDA[Title/Abstract]) OR (PFOSA[Title/Abstract]) OR (MeFOSAA[Title/Abstract]) OR (Methylperfluoro\*[Title/Abstract]) OR (EtFOSAA[Title/Abstract]) OR (Ethylperfluoro\*[Title/Abstract]) OR (PFBS[Title/Abstract]) OR (PFPeS[Title/Abstract]) OR (PFHxS[Title/Abstract]) OR (PFHpS[Title/Abstract]) OR (PFOS[Title/Abstract]) OR (PFNS[Title/Abstract]) OR (PFDS[Title/Abstract]) OR (FTSA[Title/Abstract]) OR (GenX[Title/Abstract]) OR (HFPO[Title/Abstract]) OR ("2,3,3,3-Tetrafluoro-2-(heptafluoropropoxy)propan\*"[Title/Abstract]) OR (C6O4[Title/Abstract]) OR (DONA[Title/Abstract]) OR (PFESA[Title/Abstract]) OR (DIOX[Title/Abstract]) OR (“F-53B”[Title/Abstract]) OR (PFECHS[Title/Abstract]) OR (PFEtCHxS[Title/Abstract]))))

**Filter: publication year from 01-01-2000 to 31-12-2022**

**Text string used for the search in Embase:**

(((('childhood obesity'/exp) OR ('obesity'/exp AND ([adolescent]/lim OR [child]/lim OR [embryo]/lim OR [fetus]/lim OR [infant]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim OR [young adult]/lim OR 'breast feeding'/exp)) OR ('body weight disorder'/exp AND ([adolescent]/lim OR [child]/lim OR [embryo]/lim OR [fetus]/lim OR [infant]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim OR [young adult]/lim OR 'breast feeding'/exp)) OR ('overnutrition'/exp AND ([adolescent]/lim OR [child]/lim OR [embryo]/lim OR [fetus]/lim OR [infant]/lim OR [newborn]/lim OR [preschool]/lim OR [school]/lim OR [young adult]/lim OR 'breast feeding'/exp))) AND ('fluorocarbon'/exp OR 'fluorinated hydrocarbon'/exp OR 'perfluoroalkanoic acid'/exp OR 'perfluoro compound'/exp OR 'organofluorine derivative'/exp OR 'perfluorobutanoic acid'/exp OR 'perfluoropentanoic acid'/exp OR 'perfluoroheptanoic acid'/exp OR 'perfluorodecanoic acid'/exp OR 'perfluorotridecanoic acid'/exp OR 'perfluorotetradecanoic acid'/exp OR 'perfluorooctanesulfonamide'/exp OR 'n ethylperfluorooctanesulfonamide'/exp OR 'perfluorobutanesulfonic acid'/exp OR 'perfluorohexanesulfonic acid'/exp OR 'perfluoroheptane sulfonic acid'/exp OR 'perfluorooctanesulfonic acid'/exp OR 'perfluorodecane sulfonic acid'/exp OR 'perfluorodecanesulfonic acid'/exp)) OR ((newborn\*:ti,ab,kw OR neonat\*:ti,ab,kw OR infan\*:ti,ab,kw OR toddler\*:ti,ab,kw OR kid:ti,ab,kw OR kids:ti,ab,kw OR baby:ti,ab,kw OR babies:ti,ab,kw OR boy:ti,ab,kw OR boys:ti,ab,kw OR girl\*:ti,ab,kw OR child\*:ti,ab,kw OR adolescen\*:ti,ab,kw OR teen\*:ti,ab,kw OR pediatr\*:ti,ab,kw OR paediatr\*:ti,ab,kw OR prenat\*:ti,ab,kw OR intrauter\*:ti,ab,kw OR pregnant\*:ti,ab,kw OR gestat\*:ti,ab,kw OR gravid\*:ti,ab,kw OR fetus:ti,ab,kw OR breastfeed\*:ti,ab,kw OR nourish:ti,ab,kw OR nursing:ti,ab,kw OR suckling:ti,ab,kw OR lactate:ti,ab,kw OR milk:ti,ab,kw) AND (Obes\*:ti,ab,kw OR Overweight\*:ti,ab,kw OR Overnutrition:ti,ab,kw OR BMI:ti,ab,kw OR “body mass index”:ti,ab,kw OR weight:ti,ab,kw OR height:ti,ab,kw OR “waist circumference”:ti,ab,kw OR WC:ti,ab,kw OR “fat mass”:ti,ab,kw OR FM:ti,ab,kw OR “body fat”:ti,ab,kw OR adipos\*:ti,ab,kw) AND (Fluorocarb\*:ti,ab,kw OR polyfluoro\*:ti,ab,kw OR perfluoro\*:ti,ab,kw OR PFAS:ti,ab,kw OR PFBA:ti,ab,kw OR PFPeA:ti,ab,kw OR PFHxA:ti,ab,kw OR PFHpA:ti,ab,kw OR PFOA:ti,ab,kw OR PFNA:ti,ab,kw OR PFDA:ti,ab,kw OR PFUnDA:ti,ab,kw OR PFDoDA:ti,ab,kw OR PFTrDA:ti,ab,kw OR PFTeDA:ti,ab,kw OR PFOSA:ti,ab,kw OR MeFOSAA:ti,ab,kw OR Methylperfluoro\*:ti,ab,kw OR EtFOSAA:ti,ab,kw OR Ethylperfluoro\*:ti,ab,kw OR PFBS:ti,ab,kw OR PFPeS:ti,ab,kw OR PFHxS:ti,ab,kw OR PFHpS:ti,ab,kw OR PFOS:ti,ab,kw OR PFNS:ti,ab,kw OR PFDS:ti,ab,kw OR FTSA:ti,ab,kw OR GenX:ti,ab,kw OR HFPO:ti,ab,kw OR "2,3,3,3-Tetrafluoro-2-heptafluoropropoxypropan\*":ti,ab,kw OR C6O4:ti,ab,kw OR DONA:ti,ab,kw OR PFESA:ti,ab,kw OR DIOX:ti,ab,kw OR “F-53B”:ti,ab,kw OR PFECHS:ti,ab,kw OR PFEtCHxS:ti,ab,kw OR '375 22 4':rn OR '2706 90 3':rn OR '307 24 4':rn OR '375 85 9':rn OR '335 67 1':rn OR '375 95 1':rn OR '335 76 2':rn OR '2058 94 8':rn OR '307 55 1':rn OR '72629 94 8':rn OR '376 06 7':rn OR '754 91 6':rn OR '2355 31 9':rn OR '2991 50 6':rn OR '375 73 5':rn OR '2706 91 4':rn OR '355 46 4':rn OR '375 92 8':rn OR '1763 23 1':rn OR '68259 12 1':rn OR '335 77 3':rn OR '757124 72 4':rn OR '27619 97 2':rn OR '39108 34 4':rn OR '13252 13 6':rn OR '1190931 41 9':rn OR '919005 14 4':rn OR '763051 92 9':rn OR '756426 58 1':rn OR '646 83 3':rn)) AND (2000:py OR 2001:py OR 2002:py OR 2003:py OR 2004:py OR 2005:py OR 2006:py OR 2007:py OR 2008:py OR 2009:py OR 2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py OR 2021:py OR 2022:py))

**R script:**

####################start of the script##############

library(tidyverse)

library(meta)

library(anthro)

library(rmeta)

library(grid)

library(gridExtra)

######### This script can be subdivided in 7 sections:

# Section 1: "Merging the databases of studies"

# Section 2: "Transforming effect estimates from studies"

# Section 3: "Performing the meta-analyses"

# Section 4: "sensitivity analysis"

# Section 5: "Meta-analyses stratified by age"

# Section 6: "Meta-analyses stratified by age - sensitivity analyses"

# Section 7: "Developing the superimposed forest plots"

####### Section 1: "Merging the databases of studies"

#### In this section, articles from PubMed and Embase were merged based on the DOI

### Loading the data obtained from the two databases:

PM\_tot <- read\_csv("Frigerio\_PFASs\_rev\_TableS01\_All\_PubMed.csv") %>%

mutate(DOI = tolower(DOI))

Em\_tot <- read\_csv("Frigerio\_PFASs\_rev\_TableS02\_All\_Embase.csv") %>%

mutate(DOI = tolower(DOI))

### creating a column with TRUE or FALSE to verify which studies are present in each other databases

PM <- PM\_tot %>%

add\_column(code = paste0("nPM", str\_pad(1:length(PM\_tot$Title), width = 3, side = "left", pad = "0")), .before = 1) %>%

mutate(pres\_in\_Em\_tot\_DOI = ifelse(is.na(DOI),NA,ifelse(DOI %in% Em\_tot$DOI, TRUE, FALSE)))

Em <- Em\_tot %>%

add\_column(code = paste0("nEm", str\_pad(1:length(Em\_tot$Title), width = 3, side = "left", pad = "0")), .before = 1) %>%

mutate(pres\_in\_PM\_tot\_DOI = ifelse(is.na(DOI),NA,ifelse(DOI %in% PM\_tot$DOI, TRUE, FALSE)))

## check if the entries to be merged are actually of the same number:

summarise(PM, pres\_Em\_DOI = sum(pres\_in\_Em\_tot\_DOI, na.rm=TRUE))

summarise(Em, pres\_PM\_DOI = sum(pres\_in\_PM\_tot\_DOI, na.rm=TRUE))

## the number is not consistent, checking where the problem is:

which(duplicated(filter(PM, pres\_in\_Em\_tot\_DOI == TRUE)$DOI))

which(duplicated(filter(Em, pres\_in\_PM\_tot\_DOI == TRUE)$DOI))

## So, it seems that there are 2 pairs of entries in the Embase database with the same DOI that don't allow a consistent merge

## Fixing the issue:

duplicates <- which(Em\_tot$DOI %in% filter(Em, pres\_in\_PM\_tot\_DOI == TRUE)$DOI[duplicated(filter(Em, pres\_in\_PM\_tot\_DOI == TRUE)$DOI)])

Em\_tot\_edit <- Em\_tot

Em\_tot\_edit$DOI[duplicates[2]] <- paste0(Em\_tot$DOI[duplicates[2]], "\_BIS")

Em\_tot\_edit$DOI[duplicates[3]] <- paste0(Em\_tot$DOI[duplicates[3]], "\_BIS")

## So, preparing the data frames again:

PM\_edit <- PM\_tot %>%

add\_column(code = paste0("nPM", str\_pad(1:length(PM\_tot$Title), width = 3, side = "left", pad = "0")), .before = 1) %>%

mutate(pres\_in\_Em\_tot\_DOI = ifelse(is.na(DOI),NA,ifelse(DOI %in% Em\_tot\_edit$DOI, TRUE, FALSE)))

Em\_edit <- Em\_tot\_edit %>%

add\_column(code = paste0("nEm", str\_pad(1:length(Em\_tot$Title), width = 3, side = "left", pad = "0")), .before = 1) %>%

mutate(pres\_in\_PM\_tot\_DOI = ifelse(is.na(DOI),NA,ifelse(DOI %in% PM\_tot$DOI, TRUE, FALSE)))

## now, check:

summarise(PM\_edit, pres\_Em\_DOI = sum(pres\_in\_Em\_tot\_DOI, na.rm=TRUE))

summarise(Em\_edit, pres\_PM\_DOI = sum(pres\_in\_PM\_tot\_DOI, na.rm=TRUE))

## now the number is consistent, we can merge:

colnames(PM\_edit) <- paste0("PM\_", colnames(PM\_edit))

colnames(Em\_edit) <- paste0("Em\_", colnames(Em\_edit))

PM\_in\_comm\_with\_Em <- filter(PM\_edit, PM\_pres\_in\_Em\_tot\_DOI == TRUE)

Em\_in\_comm\_with\_PM <- filter(Em\_edit, Em\_pres\_in\_PM\_tot\_DOI == TRUE)

PM\_not\_in\_comm\_with\_Em <- filter(PM\_edit, PM\_pres\_in\_Em\_tot\_DOI == FALSE | is.na(PM\_pres\_in\_Em\_tot\_DOI))

Em\_not\_in\_comm\_with\_PM <- filter(Em\_edit, Em\_pres\_in\_PM\_tot\_DOI == FALSE | is.na(Em\_pres\_in\_PM\_tot\_DOI))

PM\_in\_comm\_with\_Em <- arrange(PM\_in\_comm\_with\_Em, PM\_DOI)

Em\_in\_comm\_with\_PM <- arrange(Em\_in\_comm\_with\_PM, Em\_DOI)

DB\_merged1 <- cbind(PM\_in\_comm\_with\_Em, Em\_in\_comm\_with\_PM)

DB\_merged2\_left <- PM\_not\_in\_comm\_with\_Em

DB\_merged2\_right <- as\_tibble(matrix(data = rep(NA, length(PM\_not\_in\_comm\_with\_Em$PM\_code)\*length(colnames(Em\_not\_in\_comm\_with\_PM))),

nrow = length(PM\_not\_in\_comm\_with\_Em$PM\_code),

ncol = length(colnames(Em\_not\_in\_comm\_with\_PM)),

dimnames = list(NULL,

colnames(Em\_not\_in\_comm\_with\_PM))))

DB\_merged2 <- cbind(DB\_merged2\_left, DB\_merged2\_right)

DB\_merged3\_left <- as\_tibble(matrix(data = rep(NA, length(Em\_not\_in\_comm\_with\_PM$Em\_code)\*length(colnames(PM\_not\_in\_comm\_with\_Em))),

nrow = length(Em\_not\_in\_comm\_with\_PM$Em\_code),

ncol = length(colnames(PM\_not\_in\_comm\_with\_Em)),

dimnames = list(NULL,

colnames(PM\_not\_in\_comm\_with\_Em))))

DB\_merged3\_right <- Em\_not\_in\_comm\_with\_PM

DB\_merged3 <- cbind(DB\_merged3\_left, DB\_merged3\_right)

DB\_merged <- rbind(DB\_merged1, DB\_merged2, DB\_merged3)

DB\_merged <- DB\_merged %>%

arrange(PM\_code, Em\_code) %>%

add\_column(Code = paste0("n", str\_pad(1:length(DB\_merged$PM\_code), width = 3, side = "left", pad = "0")), .before = 1) %>%

arrange(Code)

write\_tsv(DB\_merged, "Frigerio\_PFASs\_rev\_PM\_Em\_studies\_merged.txt")

### This data frame was then manually modified in Excel, used for the study evaluation and inclusion, for the collection of information from studies, and for the quality of reporting. The final Excel database is reported in the Supplementary Table S03

####### End of Section 1 #######

######## Section 2: "Transforming effect estimates from studies"

#### In this section, data obtained from studies were transformed to be comparable each other

data\_extracted <- read\_tsv("Frigerio\_PFASs\_rev\_TableS04\_estr\_estim.txt")

## loading tables for z-scores

## BMI:

# from: https://www.who.int/toolkits/child-growth-standards/standards/body-mass-index-for-age-bmi-for-age

BMI\_girls\_0\_13\_w <- read\_tsv("WHO\_bmi\_girls\_0-to-13-weeks\_zscores.txt") %>% ## table downloaded from https://cdn.who.int/media/docs/default-source/child-growth/child-growth-standards/indicators/body-mass-index-for-age/bmi\_girls\_0-to-13-weeks\_zscores.xlsx?sfvrsn=7668918a\_7

mutate(Day = Week\*7)

BMI\_girls\_0\_2\_y <- read\_tsv("WHO\_bmi\_girls\_0-to-2-years\_zscores.txt") %>% ## table downloaded from https://cdn.who.int/media/docs/default-source/child-growth/child-growth-standards/indicators/body-mass-index-for-age/bmi\_girls\_0-to-2-years\_zscores.xlsx?sfvrsn=2be9859c\_7

mutate(Day = Month\*30)

BMI\_girls\_2\_5\_y <- read\_tsv("WHO\_bmi\_girls\_2-to-5-years\_zscores.txt") %>% ## table downloaded from https://cdn.who.int/media/docs/default-source/child-growth/child-growth-standards/indicators/body-mass-index-for-age/bmi\_girls\_2-to-5-years\_zscores.xlsx?sfvrsn=452aca36\_7

mutate(Day = Month\*30)

BMI\_boys\_0\_13\_w <- read\_tsv("WHO\_bmi\_boys\_0-to-13-weeks\_zscores.txt") %>% ## table downloaded from https://cdn.who.int/media/docs/default-source/child-growth/child-growth-standards/indicators/body-mass-index-for-age/bmi\_boys\_0-to-13-weeks\_zscores.xlsx?sfvrsn=8eff3d30\_7

mutate(Day = Week\*7)

BMI\_boys\_0\_2\_y <- read\_tsv("WHO\_bmi\_boys\_0-to-2-years\_zcores.txt") %>% ## table downloaded from https://cdn.who.int/media/docs/default-source/child-growth/child-growth-standards/indicators/body-mass-index-for-age/bmi\_boys\_0-to-2-years\_zcores.xlsx?sfvrsn=df725cc9\_7

mutate(Day = Month\*30)

BMI\_boys\_2\_5\_y <- read\_tsv("WHO\_bmi\_boys\_2-to-5-years\_zscores.txt") %>% ## table downloaded from https://cdn.who.int/media/docs/default-source/child-growth/child-growth-standards/indicators/body-mass-index-for-age/bmi\_boys\_2-to-5-years\_zscores.xlsx?sfvrsn=73010c9b\_5

mutate(Day = Month\*30)

# from https://www.who.int/tools/growth-reference-data-for-5to19-years/indicators/bmi-for-age

BMI\_girls\_5\_19\_y <- read\_tsv("WHO\_bmi\_girls\_5-to-19-years\_zscores.txt") %>% ## table downloaded from https://cdn.who.int/media/docs/default-source/child-growth/growth-reference-5-19-years/bmi-for-age-(5-19-years)/bmi-girls-z-who-2007-exp.xlsx?sfvrsn=79222875\_2

mutate(Day = Month\*30)

BMI\_boys\_5\_19\_y <- read\_tsv("WHO\_bmi\_boys\_5-to-19-years\_zscores.txt") %>% ## table downloaded from https://cdn.who.int/media/docs/default-source/child-growth/growth-reference-5-19-years/bmi-for-age-(5-19-years)/bmi-boys-z-who-2007-exp.xlsx?sfvrsn=a84bca93\_2

mutate(Day = Month\*30)

## WC:

# from Table S01 of Sharma, A., Metzger, D., Daymont, C. et al. LMS tables for waist-circumference and waist-height ratio Z-scores in children aged 5-19 y in NHANES III: association with cardio-metabolic risks. Pediatr Res 78, 723-729 (2015).

# https://doi.org/10.1038/pr.2015.160

WC\_girls\_5\_19\_y <- read\_tsv("Sharma\_et\_al\_WC\_girls\_5-to-19-years\_zscores.txt") %>% ## table downloaded from https://static-content.springer.com/esm/art%3A10.1038%2Fpr.2015.160/MediaObjects/41390\_2015\_BFpr2015160\_MOESM39\_ESM.xls

mutate(Day = month\*30)

WC\_boys\_5\_19\_y <- read\_tsv("Sharma\_et\_al\_WC\_boys\_5-to-19-years\_zscores.txt") %>% ## table downloaded from https://static-content.springer.com/esm/art%3A10.1038%2Fpr.2015.160/MediaObjects/41390\_2015\_BFpr2015160\_MOESM39\_ESM.xls

mutate(Day = month\*30)

## FMI:

# from Table 2 of Weber DR, Moore RH, Leonard MB, Zemel BS. Fat and lean BMI reference curves in children and adolescents and their utility in identifying excess adiposity compared with BMI and percentage body fat. Am J Clin Nutr. 2013 Jul;98(1):49-56.

# doi: 10.3945/ajcn.112.053611

FMI\_girls\_8\_20\_y <- read\_tsv("Weber\_et\_al\_FMI\_girls\_8-to-20-years\_zscores.txt") %>%

mutate(M = `50th`, Age\_to\_separate = Age) %>%

separate(col = Age\_to\_separate, into = c("Year1", "Year2"), sep = "-") %>%

mutate(Year1 = as.numeric(Year1), Year2 = as.numeric(str\_replace(Year2, " y", ""))) %>%

rowwise() %>%

mutate(Year\_mean = mean(c(Year1, Year2)), Day = Year\_mean\*365)

FMI\_boys\_8\_20\_y <- read\_tsv("Weber\_et\_al\_FMI\_boys\_8-to-20-years\_zscores.txt") %>%

mutate(M = `50th`, Age\_to\_separate = Age) %>%

separate(col = Age\_to\_separate, into = c("Year1", "Year2"), sep = "-") %>%

mutate(Year1 = as.numeric(Year1), Year2 = as.numeric(str\_replace(Year2, " y", ""))) %>%

rowwise() %>%

mutate(Year\_mean = mean(c(Year1, Year2)), Day = Year\_mean\*365)

data\_extracted\_transf <- data\_extracted %>%

# first convert the RR in OR:

mutate(estim\_v0 = estim, ci95\_lower\_v0 = ci95\_lower, ci95\_upper\_v0 = ci95\_upper) %>%

mutate(estim\_va = ifelse(outcome\_variables\_type == "RR",

(estim\_v0-overweight\_prevalence\*estim\_v0)/(1-overweight\_prevalence\*estim\_v0), estim\_v0),

ci95\_lower\_va = ifelse(outcome\_variables\_type == "RR",

(ci95\_lower\_v0-overweight\_prevalence\*ci95\_lower\_v0)/(1-overweight\_prevalence\*ci95\_lower\_v0), ci95\_lower\_v0),

ci95\_upper\_va = ifelse(outcome\_variables\_type == "RR",

(ci95\_upper\_v0-overweight\_prevalence\*ci95\_upper\_v0)/(1-overweight\_prevalence\*ci95\_upper\_v0), ci95\_upper\_v0)) %>%

# converting OR in standardized mean difference:

mutate(estim\_vb = ifelse(outcome\_variables\_type %in% c("RR", "OR"),

log10(estim\_va)\*(sqrt(3)/pi), estim\_va),

ci95\_lower\_vb = ifelse(outcome\_variables\_type %in% c("RR", "OR"),

log10(ci95\_lower\_va)\*(sqrt(3)/pi), ci95\_lower\_va),

ci95\_upper\_vb = ifelse(outcome\_variables\_type %in% c("RR", "OR"),

log10(ci95\_upper\_va)\*(sqrt(3)/pi), ci95\_upper\_va)) %>%

## then:

mutate(se\_vb = (ci95\_upper\_vb - ci95\_lower\_vb)/3.92) %>% #to calculate standard error

mutate(estim\_v1 = estim\_vb, ci95\_lower\_v1 = ci95\_lower\_vb, ci95\_upper\_v1 = ci95\_upper\_vb, se\_v1 = se\_vb) %>%

mutate(estim\_v2 = ifelse(estimate\_reported != "% change in the outcome",

ifelse(PFAS\_variable\_type == "unit", estim\_v1,

ifelse(PFAS\_variable\_type == "ln", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = exp(1))\*estim\_v1,

ifelse(PFAS\_variable\_type == "log10", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = 10)\*estim\_v1,

ifelse(PFAS\_variable\_type == "log2", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = 2)\*estim\_v1, estim\_v1)))), estim\_v1),

ci95\_lower\_v2 = ifelse(estimate\_reported != "% change in the outcome",

ifelse(PFAS\_variable\_type == "unit", estim\_v1-(1.96\*se\_v1),

ifelse(PFAS\_variable\_type == "ln", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = exp(1))\*(estim\_v1-(1.96\*se\_v1)),

ifelse(PFAS\_variable\_type == "log10", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = 10)\*(estim\_v1-(1.96\*se\_v1)),

ifelse(PFAS\_variable\_type == "log2", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = 2)\*(estim\_v1-(1.96\*se\_v1)), ci95\_lower\_v1)))), ci95\_lower\_v1),

ci95\_upper\_v2 = ifelse(estimate\_reported != "% change in the outcome",

ifelse(PFAS\_variable\_type == "unit", estim\_v1+(1.96\*se\_v1),

ifelse(PFAS\_variable\_type == "ln", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = exp(1))\*(estim\_v1+(1.96\*se\_v1)),

ifelse(PFAS\_variable\_type == "log10", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = 10)\*(estim\_v1+(1.96\*se\_v1)),

ifelse(PFAS\_variable\_type == "log2", log((1+(1/Mean\_or\_Median\_PFAS\_ngmL)), base = 2)\*(estim\_v1+(1.96\*se\_v1)), ci95\_upper\_v1)))), ci95\_upper\_v1),

estim\_v3 = ifelse(estimate\_reported == "% change in the outcome", # considering that the base of the log-transformation for Y is always e

ifelse(PFAS\_variable\_type == "unit", (exp(1)^(log((estim\_v2/100)+1))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "ln", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = exp(1))\*log((estim\_v2/100)+1))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "log10", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = 10)\*log((estim\_v2/100)+1))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "log2", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = 2)\*log((estim\_v2/100)+1))-1)\*Mean\_or\_Median\_outcome, estim\_v2)))), estim\_v2),

ci95\_lower\_v3 = ifelse(estimate\_reported == "% change in the outcome", # considering that the base of the log-transformation for Y is always e

ifelse(PFAS\_variable\_type == "unit", (exp(1)^(log((estim\_v2/100)+1)-(1.96\*log(((ci95\_upper\_v1 - ci95\_lower\_v1)/3.92/100)+1)))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "ln", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = exp(1))\*(log((estim\_v2/100)+1)-(1.96\*log(((ci95\_upper\_v1 - ci95\_lower\_v1)/3.92/100)+1))))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "log10", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = 10)\*(log((estim\_v2/100)+1)-(1.96\*log(((ci95\_upper\_v1 - ci95\_lower\_v1)/3.92/100)+1))))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "log2", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = 2)\*(log((estim\_v2/100)+1)-(1.96\*log(((ci95\_upper\_v1 - ci95\_lower\_v1)/3.92/100)+1))))-1)\*Mean\_or\_Median\_outcome, ci95\_lower\_v2)))), ci95\_lower\_v2),

ci95\_upper\_v3 = ifelse(estimate\_reported == "% change in the outcome", # considering that the base of the log-transformation for Y is always e

ifelse(PFAS\_variable\_type == "unit", (exp(1)^(log((estim\_v2/100)+1)+(1.96\*log(((ci95\_upper\_v1 - ci95\_lower\_v1)/3.92/100)+1)))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "ln", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = exp(1))\*(log((estim\_v2/100)+1)+(1.96\*log(((ci95\_upper\_v1 - ci95\_lower\_v1)/3.92/100)+1))))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "log10", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = 10)\*(log((estim\_v2/100)+1)+(1.96\*log(((ci95\_upper\_v1 - ci95\_lower\_v1)/3.92/100)+1))))-1)\*Mean\_or\_Median\_outcome,

ifelse(PFAS\_variable\_type == "log2", (exp(1)^(log(1+(1/Mean\_or\_Median\_PFAS\_ngmL), base = 2)\*(log((estim\_v2/100)+1)+(1.96\*log(((ci95\_upper\_v1 - ci95\_lower\_v1)/3.92/100)+1))))-1)\*Mean\_or\_Median\_outcome, ci95\_upper\_v2)))), ci95\_upper\_v2),

estim\_v4 = ifelse(estimate\_reported %in% c("T3vsT1", "T2vsT1", "Q4vsQ1", "Q3vsQ1", "Q2vsQ1", "change per interquartile range", "change for each SD increase"), estim\_v3/range\_ngmL, estim\_v3),

se\_v4 = ifelse(estimate\_reported %in% c("T3vsT1", "T2vsT1", "Q4vsQ1", "Q3vsQ1", "Q2vsQ1", "change per interquartile range", "change for each SD increase"), ((ci95\_upper\_v3 - ci95\_lower\_v3)/3.92)/range\_ngmL, (ci95\_upper\_v3 - ci95\_lower\_v3)/3.92),

ci95\_lower\_v4 = estim\_v4-(1.96\*se\_v4),

ci95\_upper\_v4 = estim\_v4+(1.96\*se\_v4),

Calc\_BMI\_zscore = NA,

Calc\_WC\_zscore = NA,

Calc\_FMI\_zscore = NA,

estim\_v5 = NA,

se\_v5 = NA,

ci95\_lower\_v5 = NA,

ci95\_upper\_v5 = NA)

for (i in 1:length(data\_extracted\_transf$META)) {

compute\_zscore <- function(zscoretable, Y) {

vect <- zscoretable$Day

my\_number <- data\_extracted\_transf$age\_in\_days[i]

ref\_zscore\_table <- which(abs(vect-my\_number)==min(abs(vect-my\_number)))

return(anthro\_api\_compute\_zscore(y = Y,

m = zscoretable$M[ref\_zscore\_table],

l = zscoretable$L[ref\_zscore\_table],

s = zscoretable$S[ref\_zscore\_table]))

}

out\_data <- data\_extracted\_transf$Mean\_or\_Median\_outcome[i]

if (data\_extracted\_transf$outcome\_variables\_type[i] == "BMI (kg/m2)") {

if (data\_extracted\_transf$age\_in\_days[i] < 7\*13) {

if (data\_extracted\_transf$sex[i] == "girls") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- compute\_zscore(BMI\_girls\_0\_13\_w, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "boys") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- compute\_zscore(BMI\_boys\_0\_13\_w, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "both\_sexes") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- mean(c(compute\_zscore(BMI\_girls\_0\_13\_w, Y = out\_data), compute\_zscore(BMI\_boys\_0\_13\_w, Y = out\_data)))

}

} else if (data\_extracted\_transf$age\_in\_days[i] < 365\*2) {

if (data\_extracted\_transf$sex[i] == "girls") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- compute\_zscore(BMI\_girls\_0\_2\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "boys") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- compute\_zscore(BMI\_boys\_0\_2\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "both\_sexes") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- mean(c(compute\_zscore(BMI\_girls\_0\_2\_y, Y = out\_data), compute\_zscore(BMI\_boys\_0\_2\_y, Y = out\_data)))

}

} else if (data\_extracted\_transf$age\_in\_days[i] < 365\*5) {

if (data\_extracted\_transf$sex[i] == "girls") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- compute\_zscore(BMI\_girls\_2\_5\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "boys") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- compute\_zscore(BMI\_boys\_2\_5\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "both\_sexes") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- mean(c(compute\_zscore(BMI\_girls\_2\_5\_y, Y = out\_data), compute\_zscore(BMI\_boys\_2\_5\_y, Y = out\_data)))

}

} else if (data\_extracted\_transf$age\_in\_days[i] < 365\*19) {

if (data\_extracted\_transf$sex[i] == "girls") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- compute\_zscore(BMI\_girls\_5\_19\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "boys") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- compute\_zscore(BMI\_boys\_5\_19\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "both\_sexes") {

data\_extracted\_transf$Calc\_BMI\_zscore[i] <- mean(c(compute\_zscore(BMI\_girls\_5\_19\_y, Y = out\_data), compute\_zscore(BMI\_boys\_5\_19\_y, Y = out\_data)))

}

}

data\_extracted\_transf$estim\_v5[i] <- (data\_extracted\_transf$Calc\_BMI\_zscore[i]\*data\_extracted\_transf$estim\_v4[i])/data\_extracted\_transf$Mean\_or\_Median\_outcome[i]

data\_extracted\_transf$se\_v5[i] <- abs((data\_extracted\_transf$Calc\_BMI\_zscore[i]\*data\_extracted\_transf$se\_v4[i])/data\_extracted\_transf$Mean\_or\_Median\_outcome[i])

data\_extracted\_transf$ci95\_lower\_v5[i] <- data\_extracted\_transf$estim\_v5[i]-(1.96\*data\_extracted\_transf$se\_v5[i])

data\_extracted\_transf$ci95\_upper\_v5[i] <- data\_extracted\_transf$estim\_v5[i]+(1.96\*data\_extracted\_transf$se\_v5[i])

} else if (data\_extracted\_transf$outcome\_variables\_type[i] == "WC (cm)") {

if (data\_extracted\_transf$sex[i] == "girls") {

data\_extracted\_transf$Calc\_WC\_zscore[i] <- compute\_zscore(WC\_girls\_5\_19\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "boys") {

data\_extracted\_transf$Calc\_WC\_zscore[i] <- compute\_zscore(WC\_boys\_5\_19\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "both\_sexes") {

data\_extracted\_transf$Calc\_WC\_zscore[i] <- mean(c(compute\_zscore(WC\_girls\_5\_19\_y, Y = out\_data), compute\_zscore(WC\_boys\_5\_19\_y, Y = out\_data)))

}

data\_extracted\_transf$estim\_v5[i] <- (data\_extracted\_transf$Calc\_WC\_zscore[i]\*data\_extracted\_transf$estim\_v4[i])/data\_extracted\_transf$Mean\_or\_Median\_outcome[i]

data\_extracted\_transf$se\_v5[i] <- abs((data\_extracted\_transf$Calc\_WC\_zscore[i]\*data\_extracted\_transf$se\_v4[i])/data\_extracted\_transf$Mean\_or\_Median\_outcome[i])

data\_extracted\_transf$ci95\_lower\_v5[i] <- data\_extracted\_transf$estim\_v5[i]-(1.96\*data\_extracted\_transf$se\_v5[i])

data\_extracted\_transf$ci95\_upper\_v5[i] <- data\_extracted\_transf$estim\_v5[i]+(1.96\*data\_extracted\_transf$se\_v5[i])

} else if (data\_extracted\_transf$outcome\_variables\_type[i] == "DXA total fat mass index (kg/m2)") {

if (data\_extracted\_transf$sex[i] == "girls") {

data\_extracted\_transf$Calc\_FMI\_zscore[i] <- compute\_zscore(FMI\_girls\_8\_20\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "boys") {

data\_extracted\_transf$Calc\_FMI\_zscore[i] <- compute\_zscore(FMI\_boys\_8\_20\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "both\_sexes") {

data\_extracted\_transf$Calc\_FMI\_zscore[i] <- mean(c(compute\_zscore(FMI\_girls\_8\_20\_y, Y = out\_data), compute\_zscore(FMI\_boys\_8\_20\_y, Y = out\_data)))

}

data\_extracted\_transf$estim\_v5[i] <- (data\_extracted\_transf$Calc\_FMI\_zscore[i]\*data\_extracted\_transf$estim\_v4[i])/data\_extracted\_transf$Mean\_or\_Median\_outcome[i]

data\_extracted\_transf$se\_v5[i] <- abs((data\_extracted\_transf$Calc\_FMI\_zscore[i]\*data\_extracted\_transf$se\_v4[i])/data\_extracted\_transf$Mean\_or\_Median\_outcome[i])

data\_extracted\_transf$ci95\_lower\_v5[i] <- data\_extracted\_transf$estim\_v5[i]-(1.96\*data\_extracted\_transf$se\_v5[i])

data\_extracted\_transf$ci95\_upper\_v5[i] <- data\_extracted\_transf$estim\_v5[i]+(1.96\*data\_extracted\_transf$se\_v5[i])

} else if (data\_extracted\_transf$outcome\_variables\_type[i] == "DXA-total body fat (%)") {

out\_data <- (data\_extracted\_transf$Mean\_or\_Median\_outcome[i]/100)\*data\_extracted\_transf$furhter\_bmi[i]

if (data\_extracted\_transf$sex[i] == "girls") {

data\_extracted\_transf$Calc\_FMI\_zscore[i] <- compute\_zscore(FMI\_girls\_8\_20\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "boys") {

data\_extracted\_transf$Calc\_FMI\_zscore[i] <- compute\_zscore(FMI\_boys\_8\_20\_y, Y = out\_data)

} else if (data\_extracted\_transf$sex[i] == "both\_sexes") {

data\_extracted\_transf$Calc\_FMI\_zscore[i] <- mean(c(compute\_zscore(FMI\_girls\_8\_20\_y, Y = out\_data), compute\_zscore(FMI\_boys\_8\_20\_y, Y = out\_data)))

}

data\_extracted\_transf$estim\_v5[i] <- (data\_extracted\_transf$Calc\_FMI\_zscore[i]\*data\_extracted\_transf$estim\_v4[i])/out\_data

data\_extracted\_transf$se\_v5[i] <- abs((data\_extracted\_transf$Calc\_FMI\_zscore[i]\*data\_extracted\_transf$se\_v4[i])/out\_data)

data\_extracted\_transf$ci95\_lower\_v5[i] <- data\_extracted\_transf$estim\_v5[i]-(1.96\*data\_extracted\_transf$se\_v5[i])

data\_extracted\_transf$ci95\_upper\_v5[i] <- data\_extracted\_transf$estim\_v5[i]+(1.96\*data\_extracted\_transf$se\_v5[i])

} else {

data\_extracted\_transf$estim\_v5[i] <- data\_extracted\_transf$estim\_v4[i]

data\_extracted\_transf$se\_v5[i] <- data\_extracted\_transf$se\_v4[i]

data\_extracted\_transf$ci95\_lower\_v5[i] <- data\_extracted\_transf$ci95\_lower\_v4[i]

data\_extracted\_transf$ci95\_upper\_v5[i] <- data\_extracted\_transf$ci95\_upper\_v4[i]

}

}

data\_extracted\_transf <- mutate(data\_extracted\_transf, estim = estim\_v5, ci95\_lower = ci95\_lower\_v5, ci95\_upper = ci95\_upper\_v5, se = se\_v5)

write\_tsv(data\_extracted\_transf, "Frigerio\_PFASs\_rev\_TableS05\_transf\_estim.txt")

## This table is reported in supplementary material, Table S05

##### end of section 2 ######

######## Section 3: "Performing the meta-analyses"

#### In this section, a function was built to obtain the forest and funnel plots from each combination of exposure and outcome, besides storing the results of the meta-analysis in an object called "[...]\_meta"

### creating the function to perform the meta-analyses (forest plots and funnel-plots) and to store the results in an object called "[...]\_meta\_inv\_var" and "[...]\_meta\_subjects\_weighted"

Performing\_meta\_analysis <- function(DF, num\_to\_add = "") {

meta\_df <- metagen(data = DF,

TE = estim,

studlab = study,

random = TRUE,

fixed = TRUE,

method.tau = "REML",

n.e = n\_subj,

lower = ci95\_lower,

upper = ci95\_upper

)

assign(paste0(num\_to\_add, deparse(substitute(DF)), "\_iv"), meta\_df, envir = globalenv())

meta\_subj\_wgtd <- meta.summaries(d = DF$estim,

se = DF$se,

method="random",

weights=DF$n\_subj,

names = DF$study)

assign(paste0(num\_to\_add, deparse(substitute(DF)), "\_sw"), meta\_subj\_wgtd, envir = globalenv())

forest.meta(meta\_df,

fixed = TRUE,

random = TRUE,

leftcols = c("studlab", "age\_measurament", "age\_outcome", "n\_subj"),

leftlabs = c("Study", "Sampling", "Outcome", "Subj"),

col.square = "dark blue",

col.inside = "dark blue",

col.diamond.fixed = "orange",

col.diamond.random = "red",

col.fixed = "orange",

col.random = "red",

smlab = str\_replace\_all(deparse(substitute(DF)), "\_", " ")

)

dev.print(png, paste0("Frigerio\_", num\_to\_add, deparse(substitute(DF)), "\_Forest\_iv.png"), width=1000, height=460)

tabletext <- cbind(c("Study", DF$study, NA, "Summary"),

c("Sampling", DF$age\_measurament, NA, NA),

c("Outcome", DF$age\_outcome, NA, NA),

c("Subjects", DF$n\_subj, NA, NA),

c("Estimate [95% CI]", paste0(format(round(DF$estim, 3), nsmall = 3), " [", format(round(DF$ci95\_lower, 3), nsmall = 3), "; ", format(round(DF$ci95\_upper, 3), nsmall = 3), "]"), NA, paste0(format(round(meta\_subj\_wgtd[["summary"]], 3), nsmall = 3), " [", format(round(meta\_subj\_wgtd[["summary"]]-(meta\_subj\_wgtd[["se.summary"]]\*1.96), 3), nsmall = 3), "; ", format(round(meta\_subj\_wgtd[["summary"]]+(meta\_subj\_wgtd[["se.summary"]]\*1.96), 3), nsmall = 3), "]")))

forestplot(labeltext = tabletext,

mean = c(NA, DF$estim, NA, meta\_subj\_wgtd[["summary"]]),

lower = c(NA, DF$ci95\_lower, NA, meta\_subj\_wgtd[["summary"]]-(meta\_subj\_wgtd[["se.summary"]]\*1.96)),

upper = c(NA, DF$ci95\_upper, NA, meta\_subj\_wgtd[["summary"]]+(meta\_subj\_wgtd[["se.summary"]]\*1.96)),

align = NULL,

is.summary = c(TRUE, rep(FALSE, length(DF$estim)), FALSE, TRUE),

boxsize = c(NA, 4\*(meta\_subj\_wgtd[["weights"]]/sum(meta\_subj\_wgtd[["weights"]])), NA, 1),

col = meta.colors(box="dark blue", summary="red"))

dev.print(png, paste0("Frigerio\_", num\_to\_add, deparse(substitute(DF)), "\_Forest\_sw.png"), width=1000, height=460)

Bias\_results <- metabias(meta\_df, method.bias = "Egger", k.min = length(DF$study))

funnel.meta(meta\_df,

col = "blue",

col.random = "red",

col.fixed = "blue"

)

mtext(text = str\_replace\_all(deparse(substitute(DF)), "\_", " "),

side = 3,

line = 0,

adj = 0.8,

cex=1.3,

padj = 3,

font =2 )

mtext(text = paste0("Egger's test",

"\nt = ", round(Bias\_results$statistic, digits = 3),

"\ndf = ", Bias\_results$DF,

"\np-value = ", round(Bias\_results$pval, digits = 3),

"\n\nEstimate\nbias = ", round(Bias\_results$estimate["bias"], digits = 3),

"\nse bias = ", round(Bias\_results$estimate["se.bias"], digits = 3),

"\nintercept = ", round(Bias\_results$estimate["intercept"], digits = 3),

"\nse intercept = ", round(Bias\_results$estimate["se.intercept"], digits = 3)),

side = 3,

line = 0,

adj = 0.8,

cex=1.3,

padj = 1.35)

dev.print(png, paste0("Frigerio\_", num\_to\_add, deparse(substitute(DF)), "\_Funnel.png"), width=1000, height=800)

}

### apply the function to obtain the results of the meta-analyses:

wanted\_order <- c("PFOA\_prenatal\_BMI\_both\_sexes", "PFOA\_prenatal\_BMI\_boys", "PFOA\_prenatal\_BMI\_girls", "PFOS\_prenatal\_BMI\_both\_sexes", "PFOS\_prenatal\_BMI\_boys", "PFOS\_prenatal\_BMI\_girls", "PFHxS\_prenatal\_BMI\_both\_sexes", "PFHxS\_prenatal\_BMI\_boys", "PFHxS\_prenatal\_BMI\_girls", "PFNA\_prenatal\_BMI\_both\_sexes", "PFNA\_prenatal\_BMI\_boys", "PFNA\_prenatal\_BMI\_girls", "PFDA\_prenatal\_BMI\_both\_sexes", "PFDA\_prenatal\_BMI\_boys", "PFDA\_prenatal\_BMI\_girls", "PFUA\_prenatal\_BMI\_both\_sexes", "PFUA\_prenatal\_BMI\_boys", "PFUA\_prenatal\_BMI\_girls", "PFHpA\_prenatal\_BMI\_both\_sexes", "PFHpA\_prenatal\_BMI\_boys", "PFHpA\_prenatal\_BMI\_girls", "PFUnDA\_prenatal\_BMI\_both\_sexes", "PFUnDA\_prenatal\_BMI\_boys", "PFUnDA\_prenatal\_BMI\_girls", "MeFOSAA\_prenatal\_BMI\_both\_sexes", "MeFOSAA\_prenatal\_BMI\_boys", "MeFOSAA\_prenatal\_BMI\_girls", "PFDoA\_prenatal\_BMI\_both\_sexes", "PFDoA\_prenatal\_BMI\_boys", "PFDoA\_prenatal\_BMI\_girls", "PFOSA\_prenatal\_BMI\_both\_sexes", "PFOSA\_prenatal\_BMI\_boys", "PFOSA\_prenatal\_BMI\_girls", "PFBS\_prenatal\_BMI\_both\_sexes", "PFBS\_prenatal\_BMI\_boys", "PFBS\_prenatal\_BMI\_girls",

"PFOA\_prenatal\_risk\_both\_sexes", "PFOA\_prenatal\_risk\_boys", "PFOA\_prenatal\_risk\_girls", "PFOS\_prenatal\_risk\_both\_sexes", "PFOS\_prenatal\_risk\_boys", "PFOS\_prenatal\_risk\_girls", "PFHxS\_prenatal\_risk\_both\_sexes", "PFHxS\_prenatal\_risk\_boys", "PFHxS\_prenatal\_risk\_girls", "PFNA\_prenatal\_risk\_both\_sexes", "PFNA\_prenatal\_risk\_boys", "PFNA\_prenatal\_risk\_girls", "PFDA\_prenatal\_risk\_both\_sexes", "PFDA\_prenatal\_risk\_boys", "PFDA\_prenatal\_risk\_girls", "PFUA\_prenatal\_risk\_both\_sexes", "PFUA\_prenatal\_risk\_boys", "PFUA\_prenatal\_risk\_girls", "PFHpA\_prenatal\_risk\_both\_sexes", "PFHpA\_prenatal\_risk\_boys", "PFHpA\_prenatal\_risk\_girls", "PFUnDA\_prenatal\_risk\_both\_sexes", "PFUnDA\_prenatal\_risk\_boys", "PFUnDA\_prenatal\_risk\_girls", "MeFOSAA\_prenatal\_risk\_both\_sexes", "MeFOSAA\_prenatal\_risk\_boys", "MeFOSAA\_prenatal\_risk\_girls", "PFDoA\_prenatal\_risk\_both\_sexes", "PFDoA\_prenatal\_risk\_boys", "PFDoA\_prenatal\_risk\_girls", "PFOSA\_prenatal\_risk\_both\_sexes", "PFOSA\_prenatal\_risk\_boys", "PFOSA\_prenatal\_risk\_girls", "PFBS\_prenatal\_risk\_both\_sexes", "PFBS\_prenatal\_risk\_boys", "PFBS\_prenatal\_risk\_girls",

"PFOA\_prenatal\_WC\_both\_sexes", "PFOA\_prenatal\_WC\_boys", "PFOA\_prenatal\_WC\_girls", "PFOS\_prenatal\_WC\_both\_sexes", "PFOS\_prenatal\_WC\_boys", "PFOS\_prenatal\_WC\_girls", "PFHxS\_prenatal\_WC\_both\_sexes", "PFHxS\_prenatal\_WC\_boys", "PFHxS\_prenatal\_WC\_girls", "PFNA\_prenatal\_WC\_both\_sexes", "PFNA\_prenatal\_WC\_boys", "PFNA\_prenatal\_WC\_girls", "PFDA\_prenatal\_WC\_both\_sexes", "PFDA\_prenatal\_WC\_boys", "PFDA\_prenatal\_WC\_girls", "PFUA\_prenatal\_WC\_both\_sexes", "PFUA\_prenatal\_WC\_boys", "PFUA\_prenatal\_WC\_girls", "PFHpA\_prenatal\_WC\_both\_sexes", "PFHpA\_prenatal\_WC\_boys", "PFHpA\_prenatal\_WC\_girls", "PFUnDA\_prenatal\_WC\_both\_sexes", "PFUnDA\_prenatal\_WC\_boys", "PFUnDA\_prenatal\_WC\_girls", "MeFOSAA\_prenatal\_WC\_both\_sexes", "MeFOSAA\_prenatal\_WC\_boys", "MeFOSAA\_prenatal\_WC\_girls", "PFDoA\_prenatal\_WC\_both\_sexes", "PFDoA\_prenatal\_WC\_boys", "PFDoA\_prenatal\_WC\_girls", "PFOSA\_prenatal\_WC\_both\_sexes", "PFOSA\_prenatal\_WC\_boys", "PFOSA\_prenatal\_WC\_girls", "PFBS\_prenatal\_WC\_both\_sexes", "PFBS\_prenatal\_WC\_boys", "PFBS\_prenatal\_WC\_girls",

"PFOA\_prenatal\_DXA\_both\_sexes", "PFOA\_prenatal\_DXA\_boys", "PFOA\_prenatal\_DXA\_girls", "PFOS\_prenatal\_DXA\_both\_sexes", "PFOS\_prenatal\_DXA\_boys", "PFOS\_prenatal\_DXA\_girls", "PFHxS\_prenatal\_DXA\_both\_sexes", "PFHxS\_prenatal\_DXA\_boys", "PFHxS\_prenatal\_DXA\_girls", "PFNA\_prenatal\_DXA\_both\_sexes", "PFNA\_prenatal\_DXA\_boys", "PFNA\_prenatal\_DXA\_girls", "PFDA\_prenatal\_DXA\_both\_sexes", "PFDA\_prenatal\_DXA\_boys", "PFDA\_prenatal\_DXA\_girls", "PFUA\_prenatal\_DXA\_both\_sexes", "PFUA\_prenatal\_DXA\_boys", "PFUA\_prenatal\_DXA\_girls", "PFHpA\_prenatal\_DXA\_both\_sexes", "PFHpA\_prenatal\_DXA\_boys", "PFHpA\_prenatal\_DXA\_girls", "PFUnDA\_prenatal\_DXA\_both\_sexes", "PFUnDA\_prenatal\_DXA\_boys", "PFUnDA\_prenatal\_DXA\_girls", "MeFOSAA\_prenatal\_DXA\_both\_sexes", "MeFOSAA\_prenatal\_DXA\_boys", "MeFOSAA\_prenatal\_DXA\_girls", "PFDoA\_prenatal\_DXA\_both\_sexes", "PFDoA\_prenatal\_DXA\_boys", "PFDoA\_prenatal\_DXA\_girls", "PFOSA\_prenatal\_DXA\_both\_sexes", "PFOSA\_prenatal\_DXA\_boys", "PFOSA\_prenatal\_DXA\_girls", "PFBS\_prenatal\_DXA\_both\_sexes", "PFBS\_prenatal\_DXA\_boys", "PFBS\_prenatal\_DXA\_girls",

"PFOA\_children\_BMI\_both\_sexes", "PFOA\_children\_BMI\_boys", "PFOA\_children\_BMI\_girls", "PFOS\_children\_BMI\_both\_sexes", "PFOS\_children\_BMI\_boys", "PFOS\_children\_BMI\_girls", "PFHxS\_children\_BMI\_both\_sexes", "PFHxS\_children\_BMI\_boys", "PFHxS\_children\_BMI\_girls", "PFNA\_children\_BMI\_both\_sexes", "PFNA\_children\_BMI\_boys", "PFNA\_children\_BMI\_girls", "PFDA\_children\_BMI\_both\_sexes", "PFDA\_children\_BMI\_boys", "PFDA\_children\_BMI\_girls", "PFUA\_children\_BMI\_both\_sexes", "PFUA\_children\_BMI\_boys", "PFUA\_children\_BMI\_girls", "PFHpA\_children\_BMI\_both\_sexes", "PFHpA\_children\_BMI\_boys", "PFHpA\_children\_BMI\_girls", "PFUnDA\_children\_BMI\_both\_sexes", "PFUnDA\_children\_BMI\_boys", "PFUnDA\_children\_BMI\_girls", "MeFOSAA\_children\_BMI\_both\_sexes", "MeFOSAA\_children\_BMI\_boys", "MeFOSAA\_children\_BMI\_girls", "PFDoA\_children\_BMI\_both\_sexes", "PFDoA\_children\_BMI\_boys", "PFDoA\_children\_BMI\_girls", "PFOSA\_children\_BMI\_both\_sexes", "PFOSA\_children\_BMI\_boys", "PFOSA\_children\_BMI\_girls", "PFBS\_children\_BMI\_both\_sexes", "PFBS\_children\_BMI\_boys", "PFBS\_children\_BMI\_girls",

"PFOA\_children\_risk\_both\_sexes", "PFOA\_children\_risk\_boys", "PFOA\_children\_risk\_girls", "PFOS\_children\_risk\_both\_sexes", "PFOS\_children\_risk\_boys", "PFOS\_children\_risk\_girls", "PFHxS\_children\_risk\_both\_sexes", "PFHxS\_children\_risk\_boys", "PFHxS\_children\_risk\_girls", "PFNA\_children\_risk\_both\_sexes", "PFNA\_children\_risk\_boys", "PFNA\_children\_risk\_girls", "PFDA\_children\_risk\_both\_sexes", "PFDA\_children\_risk\_boys", "PFDA\_children\_risk\_girls", "PFUA\_children\_risk\_both\_sexes", "PFUA\_children\_risk\_boys", "PFUA\_children\_risk\_girls", "PFHpA\_children\_risk\_both\_sexes", "PFHpA\_children\_risk\_boys", "PFHpA\_children\_risk\_girls", "PFUnDA\_children\_risk\_both\_sexes", "PFUnDA\_children\_risk\_boys", "PFUnDA\_children\_risk\_girls", "MeFOSAA\_children\_risk\_both\_sexes", "MeFOSAA\_children\_risk\_boys", "MeFOSAA\_children\_risk\_girls", "PFDoA\_children\_risk\_both\_sexes", "PFDoA\_children\_risk\_boys", "PFDoA\_children\_risk\_girls", "PFOSA\_children\_risk\_both\_sexes", "PFOSA\_children\_risk\_boys", "PFOSA\_children\_risk\_girls", "PFBS\_children\_risk\_both\_sexes", "PFBS\_children\_risk\_boys", "PFBS\_children\_risk\_girls",

"PFOA\_children\_WC\_both\_sexes", "PFOA\_children\_WC\_boys", "PFOA\_children\_WC\_girls", "PFOS\_children\_WC\_both\_sexes", "PFOS\_children\_WC\_boys", "PFOS\_children\_WC\_girls", "PFHxS\_children\_WC\_both\_sexes", "PFHxS\_children\_WC\_boys", "PFHxS\_children\_WC\_girls", "PFNA\_children\_WC\_both\_sexes", "PFNA\_children\_WC\_boys", "PFNA\_children\_WC\_girls", "PFDA\_children\_WC\_both\_sexes", "PFDA\_children\_WC\_boys", "PFDA\_children\_WC\_girls", "PFUA\_children\_WC\_both\_sexes", "PFUA\_children\_WC\_boys", "PFUA\_children\_WC\_girls", "PFHpA\_children\_WC\_both\_sexes", "PFHpA\_children\_WC\_boys", "PFHpA\_children\_WC\_girls", "PFUnDA\_children\_WC\_both\_sexes", "PFUnDA\_children\_WC\_boys", "PFUnDA\_children\_WC\_girls", "MeFOSAA\_children\_WC\_both\_sexes", "MeFOSAA\_children\_WC\_boys", "MeFOSAA\_children\_WC\_girls", "PFDoA\_children\_WC\_both\_sexes", "PFDoA\_children\_WC\_boys", "PFDoA\_children\_WC\_girls", "PFOSA\_children\_WC\_both\_sexes", "PFOSA\_children\_WC\_boys", "PFOSA\_children\_WC\_girls", "PFBS\_children\_WC\_both\_sexes", "PFBS\_children\_WC\_boys", "PFBS\_children\_WC\_girls",

"PFOA\_children\_DXA\_both\_sexes", "PFOA\_children\_DXA\_boys", "PFOA\_children\_DXA\_girls", "PFOS\_children\_DXA\_both\_sexes", "PFOS\_children\_DXA\_boys", "PFOS\_children\_DXA\_girls", "PFHxS\_children\_DXA\_both\_sexes", "PFHxS\_children\_DXA\_boys", "PFHxS\_children\_DXA\_girls", "PFNA\_children\_DXA\_both\_sexes", "PFNA\_children\_DXA\_boys", "PFNA\_children\_DXA\_girls", "PFDA\_children\_DXA\_both\_sexes", "PFDA\_children\_DXA\_boys", "PFDA\_children\_DXA\_girls", "PFUA\_children\_DXA\_both\_sexes", "PFUA\_children\_DXA\_boys", "PFUA\_children\_DXA\_girls", "PFHpA\_children\_DXA\_both\_sexes", "PFHpA\_children\_DXA\_boys", "PFHpA\_children\_DXA\_girls", "PFUnDA\_children\_DXA\_both\_sexes", "PFUnDA\_children\_DXA\_boys", "PFUnDA\_children\_DXA\_girls", "MeFOSAA\_children\_DXA\_both\_sexes", "MeFOSAA\_children\_DXA\_boys", "MeFOSAA\_children\_DXA\_girls", "PFDoA\_children\_DXA\_both\_sexes", "PFDoA\_children\_DXA\_boys", "PFDoA\_children\_DXA\_girls", "PFOSA\_children\_DXA\_both\_sexes", "PFOSA\_children\_DXA\_boys", "PFOSA\_children\_DXA\_girls", "PFBS\_children\_DXA\_both\_sexes", "PFBS\_children\_DXA\_boys", "PFBS\_children\_DXA\_girls")

METAs <- wanted\_order[wanted\_order %in% unique(data\_extracted\_transf$META)]

for (a in METAs) {

number <- which(METAs == a)

number\_with\_zero <-ifelse(number<100 & number>=10, paste0("0", number), ifelse(number<10, paste0("00", number), paste0(number)))

assign(a, filter(data\_extracted\_transf, META == a))

eval(parse(text = paste0("Performing\_meta\_analysis(", a, ", num\_to\_add = 'r", number\_with\_zero, "')")))

}

### The Figures obtained are reported in the Supplementary material

####### End of Section 3 #######

##### Section 4: "sensitivity analysis" #######

## In this section, meta-analyses were repeated by excluding one study at a time.

Table\_all\_summary\_estimates <- tibble(META = character(),

studies = character(),

study\_removed = character(),

estim\_inv\_var = double(),

ci95\_lower\_inv\_var = double(),

CI95\_upper\_inv\_var = double(),

I2 = double(),

estim\_subj\_wgtd = double(),

CI95\_lower\_subj\_wgtd = double(),

CI95\_upper\_subj\_wgtd = double())

for (a in METAs) {

data\_extracted\_transf\_fil <- filter(data\_extracted\_transf, META == a)

meta\_inv\_var <- metagen(data = data\_extracted\_transf\_fil,

TE = estim,

studlab = study,

random = TRUE,

fixed = TRUE,

method.tau = "REML",

n.e = n\_subj,

lower = ci95\_lower,

upper = ci95\_upper

)

meta\_subj\_wgtd <- meta.summaries(d = data\_extracted\_transf\_fil$estim,

se = data\_extracted\_transf\_fil$se,

method="random",

weights=data\_extracted\_transf\_fil$n\_subj,

names = data\_extracted\_transf\_fil$study)

new\_row <- tibble(META = a,

studies = paste(data\_extracted\_transf\_fil$study, collapse = "; "),

study\_removed = "NONE",

estim\_inv\_var = meta\_inv\_var[["TE.random"]],

CI95\_lower\_inv\_var = meta\_inv\_var[["lower.random"]],

CI95\_upper\_inv\_var = meta\_inv\_var[["upper.random"]],

I2 = meta\_inv\_var[["I2"]],

estim\_subj\_wgtd = meta\_subj\_wgtd[["summary"]],

CI95\_lower\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]-(meta\_subj\_wgtd[["se.summary"]]\*1.96),

CI95\_upper\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]+(meta\_subj\_wgtd[["se.summary"]]\*1.96))

Table\_all\_summary\_estimates <- rbind(Table\_all\_summary\_estimates, new\_row)

studies\_vector <- data\_extracted\_transf\_fil$study

for (s in 1:length(studies\_vector)) {

study\_to\_exclude <- studies\_vector[s]

data\_extracted\_transf\_fil\_fil <- filter(data\_extracted\_transf\_fil, study != study\_to\_exclude)

meta\_inv\_var <- metagen(data = data\_extracted\_transf\_fil\_fil,

TE = estim,

studlab = study,

random = TRUE,

fixed = TRUE,

method.tau = "REML",

n.e = n\_subj,

lower = ci95\_lower,

upper = ci95\_upper

)

meta\_subj\_wgtd <- meta.summaries(d = data\_extracted\_transf\_fil\_fil$estim,

se = data\_extracted\_transf\_fil\_fil$se,

method="random",

weights=sqrt(data\_extracted\_transf\_fil\_fil$n\_subj),

names = data\_extracted\_transf\_fil\_fil$study)

new\_row <- tibble(META = a,

studies = paste(studies\_vector[-s], collapse = "; "),

study\_removed = study\_to\_exclude,

estim\_inv\_var = meta\_inv\_var[["TE.random"]],

CI95\_lower\_inv\_var = meta\_inv\_var[["lower.random"]],

CI95\_upper\_inv\_var = meta\_inv\_var[["upper.random"]],

I2 = meta\_inv\_var[["I2"]],

estim\_subj\_wgtd = meta\_subj\_wgtd[["summary"]],

CI95\_lower\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]-(meta\_subj\_wgtd[["se.summary"]]\*1.96),

CI95\_upper\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]+(meta\_subj\_wgtd[["se.summary"]]\*1.96))

Table\_all\_summary\_estimates <- rbind(Table\_all\_summary\_estimates, new\_row)

}

}

write\_tsv(Table\_all\_summary\_estimates, "Table\_all\_summary\_estimates.txt")

## This Table was further modified in Excel and reported as Table S06

####### End of Section 4 #######

##### Section 5: "Meta-analyses stratified by age" #######

## In this section, meta-analyses were performed by considering separately studies that evaluated the outcomes in children with 3 or less years old to those that evaluated the outcomes in children with more than 3 years

number\_up\_to\_now <- number

for (a in METAs) {

number <- which(METAs == a)+number\_up\_to\_now

number\_with\_zero <-ifelse(number<100 & number>=10, paste0("0", number), ifelse(number<10, paste0("00", number), paste0(number)))

assign(paste0(a, "\_0\_3y"), filter(data\_extracted\_transf, META == a, age\_in\_years <= 3))

df\_0\_3 <- filter(data\_extracted\_transf, META == a, age\_in\_years <= 3)

assign(paste0(a, "\_4\_18y"), filter(data\_extracted\_transf, META == a, age\_in\_years > 3))

df\_4\_18 <- filter(data\_extracted\_transf, META == a, age\_in\_years > 3)

if(length(df\_0\_3$META)>=3) {

eval(parse(text = paste0("Performing\_meta\_analysis(", a, "\_0\_3y, num\_to\_add = 'r", number\_with\_zero, "')")))

}

if(length(df\_4\_18$META)>=3) {

eval(parse(text = paste0("Performing\_meta\_analysis(", a, "\_4\_18y, num\_to\_add = 'r", number\_with\_zero, "')")))

}

}

### The Figures obtained are reported in the Supplementary material

####### End of Section 5 #######

##### Section 6: "Meta-analyses stratified by age - sensitivity analyses" #######

## In this section, the same meta-analyses of the previous section were performed by excluding one study at a time.

Table\_all\_summary\_estimates\_ages <- tibble(META = character(),

studies = character(),

study\_removed = character(),

estim\_inv\_var = double(),

CI95\_lower\_inv\_var = double(),

CI95\_upper\_inv\_var = double(),

I2 = double(),

estim\_subj\_wgtd = double(),

CI95\_lower\_subj\_wgtd = double(),

CI95\_upper\_subj\_wgtd = double())

for (a in METAs) {

data\_extracted\_transf\_fil\_0\_3 <- filter(data\_extracted\_transf, META == a, age\_in\_years <= 3)

if(length(data\_extracted\_transf\_fil\_0\_3$META)>=3) {

meta\_inv\_var <- metagen(data = data\_extracted\_transf\_fil\_0\_3,

TE = estim,

studlab = study,

random = TRUE,

fixed = TRUE,

method.tau = "REML",

n.e = n\_subj,

lower = ci95\_lower,

upper = ci95\_upper

)

meta\_subj\_wgtd <- meta.summaries(d = data\_extracted\_transf\_fil\_0\_3$estim,

se = data\_extracted\_transf\_fil\_0\_3$se,

method="random",

weights=data\_extracted\_transf\_fil\_0\_3$n\_subj,

names = data\_extracted\_transf\_fil\_0\_3$study)

new\_row <- tibble(META = paste0(a, "\_0\_3y"),

studies = paste(data\_extracted\_transf\_fil\_0\_3$study, collapse = "; "),

study\_removed = "NONE",

estim\_inv\_var = meta\_inv\_var[["TE.random"]],

CI95\_lower\_inv\_var = meta\_inv\_var[["lower.random"]],

CI95\_upper\_inv\_var = meta\_inv\_var[["upper.random"]],

I2 = meta\_inv\_var[["I2"]],

estim\_subj\_wgtd = meta\_subj\_wgtd[["summary"]],

CI95\_lower\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]-(meta\_subj\_wgtd[["se.summary"]]\*1.96),

CI95\_upper\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]+(meta\_subj\_wgtd[["se.summary"]]\*1.96))

Table\_all\_summary\_estimates\_ages <- rbind(Table\_all\_summary\_estimates\_ages, new\_row)

studies\_vector <- data\_extracted\_transf\_fil\_0\_3$study

for (s in 1:length(studies\_vector)) {

study\_to\_exclude <- studies\_vector[s]

data\_extracted\_transf\_fil\_fil <- filter(data\_extracted\_transf\_fil\_0\_3, study != study\_to\_exclude)

meta\_inv\_var <- metagen(data = data\_extracted\_transf\_fil\_fil,

TE = estim,

studlab = study,

random = TRUE,

fixed = TRUE,

method.tau = "REML",

n.e = n\_subj,

lower = ci95\_lower,

upper = ci95\_upper

)

meta\_subj\_wgtd <- meta.summaries(d = data\_extracted\_transf\_fil\_fil$estim,

se = data\_extracted\_transf\_fil\_fil$se,

method="random",

weights=sqrt(data\_extracted\_transf\_fil\_fil$n\_subj),

names = data\_extracted\_transf\_fil\_fil$study)

new\_row <- tibble(META = paste0(a, "\_0\_3y"),

studies = paste(studies\_vector[-s], collapse = "; "),

study\_removed = study\_to\_exclude,

estim\_inv\_var = meta\_inv\_var[["TE.random"]],

CI95\_lower\_inv\_var = meta\_inv\_var[["lower.random"]],

CI95\_upper\_inv\_var = meta\_inv\_var[["upper.random"]],

I2 = meta\_inv\_var[["I2"]],

estim\_subj\_wgtd = meta\_subj\_wgtd[["summary"]],

CI95\_lower\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]-(meta\_subj\_wgtd[["se.summary"]]\*1.96),

CI95\_upper\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]+(meta\_subj\_wgtd[["se.summary"]]\*1.96))

Table\_all\_summary\_estimates\_ages <- rbind(Table\_all\_summary\_estimates\_ages, new\_row)

}

}

data\_extracted\_transf\_fil\_4\_18 <- filter(data\_extracted\_transf, META == a, age\_in\_years > 3)

if(length(data\_extracted\_transf\_fil\_4\_18$META)>=3) {

meta\_inv\_var <- metagen(data = data\_extracted\_transf\_fil\_4\_18,

TE = estim,

studlab = study,

random = TRUE,

fixed = TRUE,

method.tau = "REML",

n.e = n\_subj,

lower = ci95\_lower,

upper = ci95\_upper

)

meta\_subj\_wgtd <- meta.summaries(d = data\_extracted\_transf\_fil\_4\_18$estim,

se = data\_extracted\_transf\_fil\_4\_18$se,

method="random",

weights=data\_extracted\_transf\_fil\_4\_18$n\_subj,

names = data\_extracted\_transf\_fil\_4\_18$study)

new\_row <- tibble(META = paste0(a, "\_4\_18y"),

studies = paste(data\_extracted\_transf\_fil\_4\_18$study, collapse = "; "),

study\_removed = "NONE",

estim\_inv\_var = meta\_inv\_var[["TE.random"]],

CI95\_lower\_inv\_var = meta\_inv\_var[["lower.random"]],

CI95\_upper\_inv\_var = meta\_inv\_var[["upper.random"]],

I2 = meta\_inv\_var[["I2"]],

estim\_subj\_wgtd = meta\_subj\_wgtd[["summary"]],

CI95\_lower\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]-(meta\_subj\_wgtd[["se.summary"]]\*1.96),

CI95\_upper\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]+(meta\_subj\_wgtd[["se.summary"]]\*1.96))

Table\_all\_summary\_estimates\_ages <- rbind(Table\_all\_summary\_estimates\_ages, new\_row)

studies\_vector <- data\_extracted\_transf\_fil\_4\_18$study

for (s in 1:length(studies\_vector)) {

study\_to\_exclude <- studies\_vector[s]

data\_extracted\_transf\_fil\_fil <- filter(data\_extracted\_transf\_fil\_4\_18, study != study\_to\_exclude)

meta\_inv\_var <- metagen(data = data\_extracted\_transf\_fil\_fil,

TE = estim,

studlab = study,

random = TRUE,

fixed = TRUE,

method.tau = "REML",

n.e = n\_subj,

lower = ci95\_lower,

upper = ci95\_upper

)

meta\_subj\_wgtd <- meta.summaries(d = data\_extracted\_transf\_fil\_fil$estim,

se = data\_extracted\_transf\_fil\_fil$se,

method="random",

weights=sqrt(data\_extracted\_transf\_fil\_fil$n\_subj),

names = data\_extracted\_transf\_fil\_fil$study)

new\_row <- tibble(META = paste0(a, "\_4\_18y"),

studies = paste(studies\_vector[-s], collapse = "; "),

study\_removed = study\_to\_exclude,

estim\_inv\_var = meta\_inv\_var[["TE.random"]],

CI95\_lower\_inv\_var = meta\_inv\_var[["lower.random"]],

CI95\_upper\_inv\_var = meta\_inv\_var[["upper.random"]],

I2 = meta\_inv\_var[["I2"]],

estim\_subj\_wgtd = meta\_subj\_wgtd[["summary"]],

CI95\_lower\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]-(meta\_subj\_wgtd[["se.summary"]]\*1.96),

CI95\_upper\_subj\_wgtd = meta\_subj\_wgtd[["summary"]]+(meta\_subj\_wgtd[["se.summary"]]\*1.96))

Table\_all\_summary\_estimates\_ages <- rbind(Table\_all\_summary\_estimates\_ages, new\_row)

}

}

}

write\_tsv(Table\_all\_summary\_estimates\_ages, "Table\_all\_summary\_estimates\_ages.txt")

## This Table was further modified in Excel and reported as Table S07

####### End of Section 6 #######

######## Section 7: "Developing the superimposed forest plots"

#### In this section, a script was carefully developed to produce graphs of superimposed forest plots

## considering data from the meta-analyses with inverse variance, all ages combined, and considering stratification by sex.

### creating the database with the information from all meta-analyses with inverse variance:

all\_objects <- ls()

iv\_metas <- all\_objects[grep("\_iv", all\_objects)]

iv\_metas\_not\_age\_stratif <- iv\_metas[!grepl("\_0\_3y", iv\_metas)]

iv\_metas\_not\_age\_stratif <- iv\_metas\_not\_age\_stratif[!grepl("\_4\_18y", iv\_metas\_not\_age\_stratif)]

list\_metasiv <- lapply(iv\_metas\_not\_age\_stratif, get)

names(list\_metasiv) <- iv\_metas\_not\_age\_stratif

all\_meta\_dataiv <- tibble(META = character(),

group = character(),

compound = character(),

outcome = character(),

sex = character(),

study = character(),

estim = double(),

lower = double(),

upper = double(),

w.random = double(),

w.random\_perc = double(),

I2 <- double())

for (l in 1:length(list\_metasiv)) {

META <- names(list\_metasiv[l])

group <- ifelse(grepl("prenatal", META, fixed = TRUE), "prenatal",

ifelse(grepl("children", META, fixed = TRUE), "children", NA))

compound <- ifelse(grepl("PFOA", META, fixed = TRUE), "PFOA",

ifelse(grepl("PFOS", META, fixed = TRUE), "PFOS",

ifelse(grepl("PFNA", META, fixed = TRUE), "PFNA",

ifelse(grepl("PFHxS", META, fixed = TRUE), "PFHxS",

ifelse(grepl("PFDA", META, fixed = TRUE), "PFDA",

ifelse(grepl("PFUA", META, fixed = TRUE), "PFUA",

ifelse(grepl("PFDoA", META, fixed = TRUE), "PFDoA",

ifelse(grepl("PFBS", META, fixed = TRUE), "PFBS", NA))))))))

outcome = ifelse(grepl("BMI", META, fixed = TRUE), "BMI",

ifelse(grepl("risk", META, fixed = TRUE), "risk",

ifelse(grepl("WC", META, fixed = TRUE), "WC",

ifelse(grepl("DXA", META, fixed = TRUE), "DXA", NA))))

sex = ifelse(grepl("both\_sexes", META, fixed = TRUE), "both\_sexes",

ifelse(grepl("boys", META, fixed = TRUE), "boys",

ifelse(grepl("girls", META, fixed = TRUE), "girls", NA)))

new\_rows <- tibble(META = rep(META, length(list\_metasiv[[l]][["studlab"]])+1),

group = rep(group, length(list\_metasiv[[l]][["studlab"]])+1),

compound = rep(compound, length(list\_metasiv[[l]][["studlab"]])+1),

outcome = rep(outcome, length(list\_metasiv[[l]][["studlab"]])+1),

sex = rep(sex, length(list\_metasiv[[l]][["studlab"]])+1),

study = c(list\_metasiv[[l]][["studlab"]], "SUMMARY"),

estim = c(list\_metasiv[[l]][["TE"]], list\_metasiv[[l]][["TE.random"]]),

lower = c(list\_metasiv[[l]][["lower"]], list\_metasiv[[l]][["lower.random"]]),

upper = c(list\_metasiv[[l]][["upper"]], list\_metasiv[[l]][["upper.random"]]),

w.random = c(list\_metasiv[[l]][["w.random"]], NA),

w.random\_perc = c(((list\_metasiv[[l]][["w.random"]]/sum(list\_metasiv[[l]][["w.random"]]))\*100), NA),

I2 = c(rep(NA, length(list\_metasiv[[l]][["studlab"]])), list\_metasiv[[l]][["I2"]]))

all\_meta\_dataiv <- rbind(all\_meta\_dataiv, new\_rows)

}

all\_meta\_dataiv <- mutate(all\_meta\_dataiv,

n\_subj = NA,

age\_measurament = NA,

age\_outcome = NA,

cohort\_name = NA,

n\_both\_sexes = NA,

n\_boys = NA,

n\_girls = NA)

for (m in 1:length(all\_meta\_dataiv$META)) {

for (e in 1:length(data\_extracted\_transf$META)) {

if(all\_meta\_dataiv$study[m] == data\_extracted\_transf$study[e] &

all\_meta\_dataiv$group[m] == data\_extracted\_transf$sampling\_time[e] &

all\_meta\_dataiv$compound[m] == data\_extracted\_transf$compound[e] &

all\_meta\_dataiv$outcome[m] == data\_extracted\_transf$outcome[e] &

all\_meta\_dataiv$sex[m] == data\_extracted\_transf$sex[e]) {

all\_meta\_dataiv$n\_subj[m] <- data\_extracted\_transf$n\_subj[e]

all\_meta\_dataiv$age\_measurament[m] <- data\_extracted\_transf$age\_measurament[e]

all\_meta\_dataiv$age\_outcome[m] <- data\_extracted\_transf$age\_outcome[e]

all\_meta\_dataiv$cohort\_name[m] <- data\_extracted\_transf$cohort\_name[e]

both\_sexes\_index <- which(data\_extracted\_transf$sex == "both\_sexes" &

all\_meta\_dataiv$study[m] == data\_extracted\_transf$study &

all\_meta\_dataiv$group[m] == data\_extracted\_transf$sampling\_time &

all\_meta\_dataiv$compound[m] == data\_extracted\_transf$compound &

all\_meta\_dataiv$outcome[m] == data\_extracted\_transf$outcome)

boys\_index <- which(data\_extracted\_transf$sex == "boys" &

all\_meta\_dataiv$study[m] == data\_extracted\_transf$study &

all\_meta\_dataiv$group[m] == data\_extracted\_transf$sampling\_time &

all\_meta\_dataiv$compound[m] == data\_extracted\_transf$compound &

all\_meta\_dataiv$outcome[m] == data\_extracted\_transf$outcome)

girls\_index <- which(data\_extracted\_transf$sex == "girls" &

all\_meta\_dataiv$study[m] == data\_extracted\_transf$study &

all\_meta\_dataiv$group[m] == data\_extracted\_transf$sampling\_time &

all\_meta\_dataiv$compound[m] == data\_extracted\_transf$compound &

all\_meta\_dataiv$outcome[m] == data\_extracted\_transf$outcome)

if (length(both\_sexes\_index) == 0) {

all\_meta\_dataiv$n\_both\_sexes[m] <- NA

} else if (length(both\_sexes\_index) == 1) {

all\_meta\_dataiv$n\_both\_sexes[m] <- data\_extracted\_transf$n\_subj[both\_sexes\_index]

} else if (length(both\_sexes\_index) > 1) {

stop("something wrong")

}

if (length(boys\_index) == 0) {

all\_meta\_dataiv$n\_boys[m] <- NA

} else if (length(boys\_index) == 1) {

all\_meta\_dataiv$n\_boys[m] <- data\_extracted\_transf$n\_subj[boys\_index]

} else if (length(boys\_index) > 1) {

stop("something wrong")

}

if (length(girls\_index) == 0) {

all\_meta\_dataiv$n\_girls[m] <- NA

} else if (length(girls\_index) == 1) {

all\_meta\_dataiv$n\_girls[m] <- data\_extracted\_transf$n\_subj[girls\_index]

} else if (length(girls\_index) > 1) {

stop("something wrong")

}

}

}

}

all\_studies <- unique(data\_extracted\_transf$study)

wanted\_order\_studies <- c(all\_studies, "SUMMARY")

## formula to build graph for each molecule:

generate\_combined\_forest <- function(all\_meta\_data, meta\_num, molecules\_to\_consider, outcome\_to\_consider, group\_to\_consider) {

all\_meta\_dataiv\_specif <- filter(all\_meta\_data, group == group\_to\_consider, compound == molecules\_to\_consider, outcome == outcome\_to\_consider)

specif\_studies <- wanted\_order\_studies[wanted\_order\_studies %in% unique(all\_meta\_dataiv\_specif$study)]

all\_meta\_dataiv\_specif <- mutate(all\_meta\_dataiv\_specif, num\_pos = NA, num\_pos\_jit = NA)

for (p in 1:length(all\_meta\_dataiv\_specif$META)) {

all\_meta\_dataiv\_specif$num\_pos[p] <- which(specif\_studies == all\_meta\_dataiv\_specif$study[p])

if(length(unique(all\_meta\_dataiv\_specif$sex))==1) {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p]

} else if (length(unique(all\_meta\_dataiv\_specif$sex))==2) {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p]

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[1]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] - 0.1 }

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[2]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] + 0.1 }

} else if (length(unique(all\_meta\_dataiv\_specif$sex))==3) {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p]

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[1]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] - 0.15 }

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[2]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] }

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[3]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] + 0.15 }

} else if (length(unique(all\_meta\_dataiv\_specif$sex))>3) {

stop("something wrong")

}

if (all\_meta\_dataiv\_specif$study[p] == "SUMMARY" & all\_meta\_dataiv\_specif$sex[p] == "both\_sexes") {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p]

} else if (all\_meta\_dataiv\_specif$study[p] == "SUMMARY" & all\_meta\_dataiv\_specif$sex[p] == "boys") {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p] + 1

} else if (all\_meta\_dataiv\_specif$study[p] == "SUMMARY" & all\_meta\_dataiv\_specif$sex[p] == "girls") {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p] + 2

}

}

all\_meta\_dataiv\_specif$num\_pos <- all\_meta\_dataiv\_specif$num\_pos\*(-1)

all\_meta\_dataiv\_specif$num\_pos\_jit <- all\_meta\_dataiv\_specif$num\_pos\_jit\*(-1)

## preparing the data to show the diamonds of the pooled estimates in the graph for prenatal exposure:

diamond\_y <- c(-0.4, 0, 0.4, 0)

index\_summary\_both\_sex <- which(all\_meta\_dataiv\_specif$sex == "both\_sexes" & all\_meta\_dataiv\_specif$study == "SUMMARY")

index\_summary\_boys <- which(all\_meta\_dataiv\_specif$sex == "boys" & all\_meta\_dataiv\_specif$study == "SUMMARY")

index\_summary\_girls <- which(all\_meta\_dataiv\_specif$sex == "girls" & all\_meta\_dataiv\_specif$study == "SUMMARY")

if (length(index\_summary\_both\_sex) != 1) {stop("Something wrong")}

if (length(index\_summary\_boys) == 0 | length(index\_summary\_girls) == 0) {

diamonds\_specif <- tibble(

TE = c(all\_meta\_dataiv\_specif$estim[index\_summary\_both\_sex], all\_meta\_dataiv\_specif$upper[index\_summary\_both\_sex], all\_meta\_dataiv\_specif$estim[index\_summary\_both\_sex], all\_meta\_dataiv\_specif$lower[index\_summary\_both\_sex]),

sex = c(rep("both\_sexes", 4)),

pos\_diam = c(all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]-diamond\_y[1],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]-diamond\_y[2],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]-diamond\_y[3],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]-diamond\_y[4]

)

)

dat\_text\_specif <- tibble(sex = c("both\_sexes"),

pos\_x = rep(0.09\*(max(all\_meta\_dataiv\_specif$upper)-min(all\_meta\_dataiv\_specif$lower)), 1),

pos\_y = c(all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]),

text = c(paste0(formatC(all\_meta\_dataiv\_specif$estim[index\_summary\_both\_sex], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif$lower[index\_summary\_both\_sex], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif$upper[index\_summary\_both\_sex], format = "f", digits = 4), "]")))

dat\_textI2\_specif <- tibble(sex = c("both\_sexes"),

pos\_x = rep(min(all\_meta\_dataiv\_specif$lower), 1),

pos\_y = c(all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]),

text = c(paste0("I^2", " = ", formatC(all\_meta\_dataiv\_specif$I2[index\_summary\_both\_sex], format = "f", digits = 2))

))

} else {

diamonds\_specif <- tibble(

TE = c(all\_meta\_dataiv\_specif$estim[index\_summary\_both\_sex], all\_meta\_dataiv\_specif$upper[index\_summary\_both\_sex], all\_meta\_dataiv\_specif$estim[index\_summary\_both\_sex], all\_meta\_dataiv\_specif$lower[index\_summary\_both\_sex],

all\_meta\_dataiv\_specif$estim[index\_summary\_boys], all\_meta\_dataiv\_specif$upper[index\_summary\_boys], all\_meta\_dataiv\_specif$estim[index\_summary\_boys], all\_meta\_dataiv\_specif$lower[index\_summary\_boys],

all\_meta\_dataiv\_specif$estim[index\_summary\_girls], all\_meta\_dataiv\_specif$upper[index\_summary\_girls], all\_meta\_dataiv\_specif$estim[index\_summary\_girls], all\_meta\_dataiv\_specif$lower[index\_summary\_girls]),

sex = c(rep("both\_sexes", 4), rep("boys", 4), rep("girls", 4)),

pos\_diam = c(all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]-diamond\_y[1],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]-diamond\_y[2],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]-diamond\_y[3],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex]-diamond\_y[4],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_boys]-diamond\_y[1],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_boys]-diamond\_y[2],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_boys]-diamond\_y[3],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_boys]-diamond\_y[4],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_girls]-diamond\_y[1],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_girls]-diamond\_y[2],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_girls]-diamond\_y[3],

all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_girls]-diamond\_y[4])

)

dat\_text\_specif <- tibble(sex = c("both\_sexes", "boys", "girls"),

pos\_x = rep(0.09\*(max(all\_meta\_dataiv\_specif$upper)-min(all\_meta\_dataiv\_specif$lower)), 3),

pos\_y = c(all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex], all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_boys], all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_girls]),

text = c(paste0(formatC(all\_meta\_dataiv\_specif$estim[index\_summary\_both\_sex], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif$lower[index\_summary\_both\_sex], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif$upper[index\_summary\_both\_sex], format = "f", digits = 4), "]"),

paste0(formatC(all\_meta\_dataiv\_specif$estim[index\_summary\_boys], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif$lower[index\_summary\_boys], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif$upper[index\_summary\_boys], format = "f", digits = 4), "]"),

paste0(formatC(all\_meta\_dataiv\_specif$estim[index\_summary\_girls], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif$lower[index\_summary\_girls], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif$upper[index\_summary\_girls], format = "f", digits = 4), "]")))

dat\_textI2\_specif <- tibble(sex = c("both\_sexes", "boys", "girls"),

pos\_x = rep(min(all\_meta\_dataiv\_specif$lower), 3),

pos\_y = c(all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_both\_sex], all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_boys], all\_meta\_dataiv\_specif$num\_pos\_jit[index\_summary\_girls]),

text = c(paste0("I^2", " = ", formatC(all\_meta\_dataiv\_specif$I2[index\_summary\_both\_sex], format = "f", digits = 2)),

paste0("I^2 = ", formatC(all\_meta\_dataiv\_specif$I2[index\_summary\_boys], format = "f", digits = 2)),

paste0("I^2 = ", formatC(all\_meta\_dataiv\_specif$I2[index\_summary\_girls], format = "f", digits = 2))))

}

# attaching together the plot with the Table of information

graph\_forest <- ggplot(data = all\_meta\_dataiv\_specif, aes(x = estim, y = num\_pos\_jit)) +

geom\_point(aes(colour = sex, fill = sex, size = w.random\_perc), shape = 22, alpha = 0.7) +

scale\_size(guide = "none") +

geom\_segment(aes(y=num\_pos\_jit, yend = num\_pos\_jit, x = lower, xend = upper, colour = sex)) +

scale\_fill\_manual(values = c("both\_sexes" = "green", "boys" = "blue", "girls" = "red")) +

scale\_colour\_manual(values = c("both\_sexes" = "green", "boys" = "blue", "girls" = "red")) +

scale\_x\_continuous(position = "top") +

geom\_vline(xintercept = 0, alpha = 0.6) +

geom\_polygon(data = diamonds\_specif, aes(x = TE, y = pos\_diam, colour = sex, fill = sex), alpha=0.7) +

geom\_text(data = dat\_text\_specif, aes(x = pos\_x, y = pos\_y, label = text), hjust = "left", size = 5) +

geom\_text(data = dat\_textI2\_specif, aes(x = pos\_x, y = pos\_y, label = text), hjust = "left", size = 5) +

theme\_classic() +

theme(axis.title.x =element\_blank(),

axis.text.x = element\_text(size=13, face="bold"),

axis.line.y=element\_blank(),

axis.title.y=element\_blank(),

axis.text.y=element\_blank(),

axis.ticks.y=element\_blank())

if(abs(min(all\_meta\_dataiv\_specif$lower))/abs(max(all\_meta\_dataiv\_specif$upper))>2 & min(all\_meta\_dataiv\_specif$lower)>0.9) {

graph\_forest <- graph\_forest + coord\_cartesian(xlim = c(-0.3, 0.3))

} else if (abs(min(all\_meta\_dataiv\_specif$lower))/abs(max(all\_meta\_dataiv\_specif$upper))>2 & min(all\_meta\_dataiv\_specif$lower)<0.9) {

graph\_forest <- graph\_forest + coord\_cartesian(xlim = c(-0.9, 0.9))

}

Table\_to\_add1 <- select(all\_meta\_dataiv\_specif, study, num\_pos) %>%

group\_by(study) %>%

slice(1) %>%

ungroup %>%

arrange(match(study, specif\_studies))

Table\_to\_add1[nrow(Table\_to\_add1) + 1 , "num\_pos"] <- -(nrow(Table\_to\_add1))-1

Table\_to\_add1[nrow(Table\_to\_add1) + 1 , "num\_pos"] <- -(nrow(Table\_to\_add1))-1

Table\_to\_add1 <- gather(Table\_to\_add1, Stat, Value, study)

graph\_table1 <- ggplot(data = Table\_to\_add1, aes(x = Stat, y = num\_pos, label = Value)) +

geom\_text(size = 5) +

scale\_x\_discrete(position = "top", labels = c("Study")) +

labs(y = NULL, x = NULL) +

theme\_classic() +

theme(axis.title.x =element\_blank(),

axis.text.x = element\_text(size=14, face="bold"),

axis.line.y=element\_blank(),

axis.title.y=element\_blank(),

axis.text.y=element\_blank(),

axis.ticks.y=element\_blank())

Table\_to\_add2 <- select(all\_meta\_dataiv\_specif, study, n\_both\_sexes, n\_boys, n\_girls, num\_pos) %>%

group\_by(study) %>%

slice(1) %>%

ungroup %>%

arrange(match(study, specif\_studies))

Table\_to\_add2[nrow(Table\_to\_add2) + 1 , "num\_pos"] <- -(nrow(Table\_to\_add2))-1

Table\_to\_add2[nrow(Table\_to\_add2) + 1 , "num\_pos"] <- -(nrow(Table\_to\_add2))-1

Table\_to\_add2 <- select(Table\_to\_add2, -study) %>%

gather(Stat, Value, n\_both\_sexes, n\_boys, n\_girls)

graph\_table2 <- ggplot(data = Table\_to\_add2, aes(x = Stat, y = num\_pos, label = Value)) +

geom\_text(size = 5) +

scale\_x\_discrete(position = "top", labels = c("both", "boys", "girls")) +

labs(y = NULL, x = NULL) +

theme\_classic() +

theme(axis.title.x =element\_blank(),

axis.text.x = element\_text(size=14, face="bold"),

axis.line.y=element\_blank(),

axis.title.y=element\_blank(),

axis.text.y=element\_blank(),

axis.ticks.y=element\_blank())

grid.arrange(graph\_table1, graph\_table2, graph\_forest ,ncol=3, widths = c(26/100,14/100, 60/100),

top = textGrob(paste0(group\_to\_consider, " exposure to ", molecules\_to\_consider, " and association with ", ifelse(outcome\_to\_consider=="risk", "risk of overweight", outcome\_to\_consider)), gp=gpar(fontsize=20, face="bold")))

dev.print(png, paste0("Frigerio\_", meta\_num, molecules\_to\_consider, group\_to\_consider, outcome\_to\_consider, ".png"), width=1000, height=abs(min(all\_meta\_dataiv\_specif$num\_pos\_jit))\*18+85)

}

## formula to create a graph combining two molecules:

generate\_combined\_forest\_by2 <- function(all\_meta\_data, meta\_num, molecules\_to\_consider, outcome\_to\_consider, group\_to\_consider) {

all\_meta\_dataiv\_specif <- filter(all\_meta\_data, group == group\_to\_consider, compound %in% molecules\_to\_consider, outcome == outcome\_to\_consider)

specif\_studies <- wanted\_order\_studies[wanted\_order\_studies %in% unique(all\_meta\_dataiv\_specif$study)]

all\_meta\_dataiv\_specif <- mutate(all\_meta\_dataiv\_specif, num\_pos = NA, num\_pos\_jit = NA)

for (p in 1:length(all\_meta\_dataiv\_specif$META)) {

all\_meta\_dataiv\_specif$num\_pos[p] <- which(specif\_studies == all\_meta\_dataiv\_specif$study[p])

if(length(unique(all\_meta\_dataiv\_specif$sex))==1) {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p]

} else if (length(unique(all\_meta\_dataiv\_specif$sex))==2) {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p]

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[1]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] - 0.1 }

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[2]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] + 0.1 }

} else if (length(unique(all\_meta\_dataiv\_specif$sex))==3) {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p]

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[1]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] - 0.15 }

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[2]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] }

if (all\_meta\_dataiv\_specif$sex[p] == unique(all\_meta\_dataiv\_specif$sex)[3]) { all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos\_jit[p] + 0.15 }

} else if (length(unique(all\_meta\_dataiv\_specif$sex))>3) {

stop("something wrong")

}

if (all\_meta\_dataiv\_specif$study[p] == "SUMMARY" & all\_meta\_dataiv\_specif$sex[p] == "both\_sexes") {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p]

} else if (all\_meta\_dataiv\_specif$study[p] == "SUMMARY" & all\_meta\_dataiv\_specif$sex[p] == "boys") {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p] + 1

} else if (all\_meta\_dataiv\_specif$study[p] == "SUMMARY" & all\_meta\_dataiv\_specif$sex[p] == "girls") {

all\_meta\_dataiv\_specif$num\_pos\_jit[p] <- all\_meta\_dataiv\_specif$num\_pos[p] + 2

}

}

all\_meta\_dataiv\_specif$num\_pos <- all\_meta\_dataiv\_specif$num\_pos\*(-1)

all\_meta\_dataiv\_specif$num\_pos\_jit <- all\_meta\_dataiv\_specif$num\_pos\_jit\*(-1)

Ylimit <- c(min(all\_meta\_dataiv\_specif$num\_pos\_jit)-0.5, max(all\_meta\_dataiv\_specif$num\_pos\_jit))

### for the first graph:

all\_meta\_dataiv\_specif1 <- filter(all\_meta\_dataiv\_specif, compound == molecules\_to\_consider[1])

diamond\_y <- c(-0.4, 0, 0.4, 0)

index\_summary\_both\_sex1 <- which(all\_meta\_dataiv\_specif1$sex == "both\_sexes" & all\_meta\_dataiv\_specif1$study == "SUMMARY")

index\_summary\_boys1 <- which(all\_meta\_dataiv\_specif1$sex == "boys" & all\_meta\_dataiv\_specif1$study == "SUMMARY")

index\_summary\_girls1 <- which(all\_meta\_dataiv\_specif1$sex == "girls" & all\_meta\_dataiv\_specif1$study == "SUMMARY")

if (length(index\_summary\_both\_sex1) != 1) {stop("Something wrong")}

if (length(index\_summary\_boys1) == 0 | length(index\_summary\_girls1) == 0) {

diamonds\_specif1 <- tibble(

TE = c(all\_meta\_dataiv\_specif1$estim[index\_summary\_both\_sex1], all\_meta\_dataiv\_specif1$upper[index\_summary\_both\_sex1], all\_meta\_dataiv\_specif1$estim[index\_summary\_both\_sex1], all\_meta\_dataiv\_specif1$lower[index\_summary\_both\_sex1]),

sex = c(rep("both\_sexes", 4)),

pos\_diam = c(all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]-diamond\_y[1],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]-diamond\_y[2],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]-diamond\_y[3],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]-diamond\_y[4]

)

)

dat\_text\_specif1 <- tibble(sex = c("both\_sexes"),

pos\_x = rep(0.09\*(max(all\_meta\_dataiv\_specif1$upper)-min(all\_meta\_dataiv\_specif1$lower)), 1),

pos\_y = c(all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]),

text = c(paste0(formatC(all\_meta\_dataiv\_specif1$estim[index\_summary\_both\_sex1], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif1$lower[index\_summary\_both\_sex1], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif1$upper[index\_summary\_both\_sex1], format = "f", digits = 4), "]")))

dat\_textI2\_specif1 <- tibble(sex = c("both\_sexes"),

pos\_x = rep(min(all\_meta\_dataiv\_specif1$lower), 1),

pos\_y = c(all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]),

text = c(paste0("I^2", " = ", formatC(all\_meta\_dataiv\_specif1$I2[index\_summary\_both\_sex1], format = "f", digits = 2))

))

} else {

diamonds\_specif1 <- tibble(

TE = c(all\_meta\_dataiv\_specif1$estim[index\_summary\_both\_sex1], all\_meta\_dataiv\_specif1$upper[index\_summary\_both\_sex1], all\_meta\_dataiv\_specif1$estim[index\_summary\_both\_sex1], all\_meta\_dataiv\_specif1$lower[index\_summary\_both\_sex1],

all\_meta\_dataiv\_specif1$estim[index\_summary\_boys1], all\_meta\_dataiv\_specif1$upper[index\_summary\_boys1], all\_meta\_dataiv\_specif1$estim[index\_summary\_boys1], all\_meta\_dataiv\_specif1$lower[index\_summary\_boys1],

all\_meta\_dataiv\_specif1$estim[index\_summary\_girls1], all\_meta\_dataiv\_specif1$upper[index\_summary\_girls1], all\_meta\_dataiv\_specif1$estim[index\_summary\_girls1], all\_meta\_dataiv\_specif1$lower[index\_summary\_girls1]),

sex = c(rep("both\_sexes", 4), rep("boys", 4), rep("girls", 4)),

pos\_diam = c(all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]-diamond\_y[1],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]-diamond\_y[2],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]-diamond\_y[3],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1]-diamond\_y[4],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_boys1]-diamond\_y[1],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_boys1]-diamond\_y[2],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_boys1]-diamond\_y[3],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_boys1]-diamond\_y[4],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_girls1]-diamond\_y[1],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_girls1]-diamond\_y[2],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_girls1]-diamond\_y[3],

all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_girls1]-diamond\_y[4])

)

dat\_text\_specif1 <- tibble(sex = c("both\_sexes", "boys", "girls"),

pos\_x = rep(0.09\*(max(all\_meta\_dataiv\_specif1$upper)-min(all\_meta\_dataiv\_specif1$lower)), 3),

pos\_y = c(all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1], all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_boys1], all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_girls1]),

text = c(paste0(formatC(all\_meta\_dataiv\_specif1$estim[index\_summary\_both\_sex1], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif1$lower[index\_summary\_both\_sex1], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif1$upper[index\_summary\_both\_sex1], format = "f", digits = 4), "]"),

paste0(formatC(all\_meta\_dataiv\_specif1$estim[index\_summary\_boys1], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif1$lower[index\_summary\_boys1], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif1$upper[index\_summary\_boys1], format = "f", digits = 4), "]"),

paste0(formatC(all\_meta\_dataiv\_specif1$estim[index\_summary\_girls1], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif1$lower[index\_summary\_girls1], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif1$upper[index\_summary\_girls1], format = "f", digits = 4), "]")))

dat\_textI2\_specif1 <- tibble(sex = c("both\_sexes", "boys", "girls"),

pos\_x = rep(min(all\_meta\_dataiv\_specif1$lower), 3),

pos\_y = c(all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_both\_sex1], all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_boys1], all\_meta\_dataiv\_specif1$num\_pos\_jit[index\_summary\_girls1]),

text = c(paste0("I^2", " = ", formatC(all\_meta\_dataiv\_specif1$I2[index\_summary\_both\_sex1], format = "f", digits = 2)),

paste0("I^2 = ", formatC(all\_meta\_dataiv\_specif1$I2[index\_summary\_boys1], format = "f", digits = 2)),

paste0("I^2 = ", formatC(all\_meta\_dataiv\_specif1$I2[index\_summary\_girls1], format = "f", digits = 2))))

}

graph\_forest1 <- ggplot(data = all\_meta\_dataiv\_specif1, aes(x = estim, y = num\_pos\_jit)) +

geom\_point(aes(colour = sex, fill = sex, size = w.random\_perc), shape = 22, alpha = 0.7) +

scale\_size(guide = "none") +

geom\_segment(aes(y=num\_pos\_jit, yend = num\_pos\_jit, x = lower, xend = upper, colour = sex)) +

scale\_fill\_manual(values = c("both\_sexes" = "green", "boys" = "blue", "girls" = "red")) +

scale\_colour\_manual(values = c("both\_sexes" = "green", "boys" = "blue", "girls" = "red")) +

scale\_x\_continuous(position = "top") +

geom\_vline(xintercept = 0, alpha = 0.6) +

geom\_polygon(data = diamonds\_specif1, aes(x = TE, y = pos\_diam, colour = sex, fill = sex), alpha=0.7) +

geom\_text(data = dat\_text\_specif1, aes(x = pos\_x, y = pos\_y, label = text), hjust = "left", size = 5) +

geom\_text(data = dat\_textI2\_specif1, aes(x = pos\_x, y = pos\_y, label = text), hjust = "left", size = 5) +

coord\_cartesian(ylim = Ylimit) +

theme\_classic() +

theme(axis.title.x =element\_blank(),

axis.text.x = element\_text(size=13, face="bold"),

axis.line.y=element\_blank(),

axis.title.y=element\_blank(),

axis.text.y=element\_blank(),

axis.ticks.y=element\_blank(),

legend.position = "none")

if(abs(min(all\_meta\_dataiv\_specif1$lower))/abs(max(all\_meta\_dataiv\_specif1$upper))>2 & min(all\_meta\_dataiv\_specif1$lower)>0.9) {

graph\_forest1 <- graph\_forest1 + coord\_cartesian(xlim = c(-0.3, 0.3))

} else if (abs(min(all\_meta\_dataiv\_specif1$lower))/abs(max(all\_meta\_dataiv\_specif1$upper))>2 & min(all\_meta\_dataiv\_specif1$lower)<0.9) {

graph\_forest1 <- graph\_forest1 + coord\_cartesian(xlim = c(-0.9, 0.9))

}

### for the second graph:

all\_meta\_dataiv\_specif2 <- filter(all\_meta\_dataiv\_specif, compound == molecules\_to\_consider[2])

diamond\_y <- c(-0.4, 0, 0.4, 0)

index\_summary\_both\_sex2 <- which(all\_meta\_dataiv\_specif2$sex == "both\_sexes" & all\_meta\_dataiv\_specif2$study == "SUMMARY")

index\_summary\_boys2 <- which(all\_meta\_dataiv\_specif2$sex == "boys" & all\_meta\_dataiv\_specif2$study == "SUMMARY")

index\_summary\_girls2 <- which(all\_meta\_dataiv\_specif2$sex == "girls" & all\_meta\_dataiv\_specif2$study == "SUMMARY")

if (length(index\_summary\_both\_sex2) != 1) {stop("Something wrong")}

if (length(index\_summary\_boys2) == 0 | length(index\_summary\_girls2) == 0) {

diamonds\_specif2 <- tibble(

TE = c(all\_meta\_dataiv\_specif2$estim[index\_summary\_both\_sex2], all\_meta\_dataiv\_specif2$upper[index\_summary\_both\_sex2], all\_meta\_dataiv\_specif2$estim[index\_summary\_both\_sex2], all\_meta\_dataiv\_specif2$lower[index\_summary\_both\_sex2]),

sex = c(rep("both\_sexes", 4)),

pos\_diam = c(all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]-diamond\_y[1],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]-diamond\_y[2],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]-diamond\_y[3],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]-diamond\_y[4]

)

)

dat\_text\_specif2 <- tibble(sex = c("both\_sexes"),

pos\_x = rep(0.09\*(max(all\_meta\_dataiv\_specif2$upper)-min(all\_meta\_dataiv\_specif2$lower)), 1),

pos\_y = c(all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]),

text = c(paste0(formatC(all\_meta\_dataiv\_specif2$estim[index\_summary\_both\_sex2], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif2$lower[index\_summary\_both\_sex2], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif2$upper[index\_summary\_both\_sex2], format = "f", digits = 4), "]")))

dat\_textI2\_specif2 <- tibble(sex = c("both\_sexes"),

pos\_x = rep(min(all\_meta\_dataiv\_specif2$lower), 1),

pos\_y = c(all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]),

text = c(paste0("I^2", " = ", formatC(all\_meta\_dataiv\_specif2$I2[index\_summary\_both\_sex2], format = "f", digits = 2))

))

} else {

diamonds\_specif2 <- tibble(

TE = c(all\_meta\_dataiv\_specif2$estim[index\_summary\_both\_sex2], all\_meta\_dataiv\_specif2$upper[index\_summary\_both\_sex2], all\_meta\_dataiv\_specif2$estim[index\_summary\_both\_sex2], all\_meta\_dataiv\_specif2$lower[index\_summary\_both\_sex2],

all\_meta\_dataiv\_specif2$estim[index\_summary\_boys2], all\_meta\_dataiv\_specif2$upper[index\_summary\_boys2], all\_meta\_dataiv\_specif2$estim[index\_summary\_boys2], all\_meta\_dataiv\_specif2$lower[index\_summary\_boys2],

all\_meta\_dataiv\_specif2$estim[index\_summary\_girls2], all\_meta\_dataiv\_specif2$upper[index\_summary\_girls2], all\_meta\_dataiv\_specif2$estim[index\_summary\_girls2], all\_meta\_dataiv\_specif2$lower[index\_summary\_girls2]),

sex = c(rep("both\_sexes", 4), rep("boys", 4), rep("girls", 4)),

pos\_diam = c(all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]-diamond\_y[1],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]-diamond\_y[2],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]-diamond\_y[3],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2]-diamond\_y[4],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_boys2]-diamond\_y[1],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_boys2]-diamond\_y[2],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_boys2]-diamond\_y[3],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_boys2]-diamond\_y[4],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_girls2]-diamond\_y[1],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_girls2]-diamond\_y[2],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_girls2]-diamond\_y[3],

all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_girls2]-diamond\_y[4])

)

dat\_text\_specif2 <- tibble(sex = c("both\_sexes", "boys", "girls"),

pos\_x = rep(0.09\*(max(all\_meta\_dataiv\_specif2$upper)-min(all\_meta\_dataiv\_specif2$lower)), 3),

pos\_y = c(all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2], all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_boys2], all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_girls2]),

text = c(paste0(formatC(all\_meta\_dataiv\_specif2$estim[index\_summary\_both\_sex2], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif2$lower[index\_summary\_both\_sex2], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif2$upper[index\_summary\_both\_sex2], format = "f", digits = 4), "]"),

paste0(formatC(all\_meta\_dataiv\_specif2$estim[index\_summary\_boys2], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif2$lower[index\_summary\_boys2], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif2$upper[index\_summary\_boys2], format = "f", digits = 4), "]"),

paste0(formatC(all\_meta\_dataiv\_specif2$estim[index\_summary\_girls2], format = "f", digits = 4), " [", formatC(all\_meta\_dataiv\_specif2$lower[index\_summary\_girls2], format = "f", digits = 4), "; ", formatC(all\_meta\_dataiv\_specif2$upper[index\_summary\_girls2], format = "f", digits = 4), "]")))

dat\_textI2\_specif2 <- tibble(sex = c("both\_sexes", "boys", "girls"),

pos\_x = rep(min(all\_meta\_dataiv\_specif2$lower), 3),

pos\_y = c(all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_both\_sex2], all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_boys2], all\_meta\_dataiv\_specif2$num\_pos\_jit[index\_summary\_girls2]),

text = c(paste0("I^2", " = ", formatC(all\_meta\_dataiv\_specif2$I2[index\_summary\_both\_sex2], format = "f", digits = 2)),

paste0("I^2 = ", formatC(all\_meta\_dataiv\_specif2$I2[index\_summary\_boys2], format = "f", digits = 2)),

paste0("I^2 = ", formatC(all\_meta\_dataiv\_specif2$I2[index\_summary\_girls2], format = "f", digits = 2))))

}

graph\_forest2 <- ggplot(data = all\_meta\_dataiv\_specif2, aes(x = estim, y = num\_pos\_jit)) +

geom\_point(aes(colour = sex, fill = sex, size = w.random\_perc), shape = 22, alpha = 0.7) +

scale\_size(guide = "none") +

geom\_segment(aes(y=num\_pos\_jit, yend = num\_pos\_jit, x = lower, xend = upper, colour = sex)) +

scale\_fill\_manual(values = c("both\_sexes" = "green", "boys" = "blue", "girls" = "red")) +

scale\_colour\_manual(values = c("both\_sexes" = "green", "boys" = "blue", "girls" = "red")) +

scale\_x\_continuous(position = "top") +

geom\_vline(xintercept = 0, alpha = 0.6) +

geom\_polygon(data = diamonds\_specif2, aes(x = TE, y = pos\_diam, colour = sex, fill = sex), alpha=0.7) +

geom\_text(data = dat\_text\_specif2, aes(x = pos\_x, y = pos\_y, label = text), hjust = "left", size = 5) +

geom\_text(data = dat\_textI2\_specif2, aes(x = pos\_x, y = pos\_y, label = text), hjust = "left", size = 5) +

coord\_cartesian(ylim = Ylimit) +

theme\_classic() +

theme(axis.title.x =element\_blank(),

axis.text.x = element\_text(size=13, face="bold"),

axis.line.y=element\_blank(),

axis.title.y=element\_blank(),

axis.text.y=element\_blank(),

axis.ticks.y=element\_blank())

if(abs(min(all\_meta\_dataiv\_specif2$lower))/abs(max(all\_meta\_dataiv\_specif2$upper))>2 & min(all\_meta\_dataiv\_specif2$lower)>0.9) {

graph\_forest2 <- graph\_forest2 + coord\_cartesian(xlim = c(-0.3, 0.3))

} else if (abs(min(all\_meta\_dataiv\_specif2$lower))/abs(max(all\_meta\_dataiv\_specif2$upper))>2 & min(all\_meta\_dataiv\_specif2$lower)<0.9) {

graph\_forest2 <- graph\_forest2 + coord\_cartesian(xlim = c(-0.9, 0.9))

}

# attaching together the plot with the Table of information

Table\_to\_add1 <- select(all\_meta\_dataiv\_specif, study, num\_pos) %>%

group\_by(study) %>%

slice(1) %>%

ungroup %>%

arrange(match(study, specif\_studies))

Table\_to\_add1[nrow(Table\_to\_add1) + 1 , "num\_pos"] <- -(nrow(Table\_to\_add1))-1

Table\_to\_add1[nrow(Table\_to\_add1) + 1 , "num\_pos"] <- -(nrow(Table\_to\_add1))-1

Table\_to\_add1 <- gather(Table\_to\_add1, Stat, Value, study)

graph\_table1 <- ggplot(data = Table\_to\_add1, aes(x = Stat, y = num\_pos, label = Value)) +

geom\_text(size = 5) +

scale\_x\_discrete(position = "top", labels = c("Study")) +

labs(y = NULL, x = NULL) +

coord\_cartesian(ylim = Ylimit) +

theme\_classic() +

theme(axis.title.x =element\_blank(),

axis.text.x = element\_text(size=14, face="bold"),

axis.line.y=element\_blank(),

axis.title.y=element\_blank(),

axis.text.y=element\_blank(),

axis.ticks.y=element\_blank())

Table\_to\_add2 <- select(all\_meta\_dataiv\_specif, study, n\_both\_sexes, n\_boys, n\_girls, num\_pos) %>%

group\_by(study) %>%

slice(1) %>%

ungroup %>%

arrange(match(study, specif\_studies))

Table\_to\_add2[nrow(Table\_to\_add2) + 1 , "num\_pos"] <- -(nrow(Table\_to\_add2))-1

Table\_to\_add2[nrow(Table\_to\_add2) + 1 , "num\_pos"] <- -(nrow(Table\_to\_add2))-1

Table\_to\_add2 <- select(Table\_to\_add2, -study) %>%

gather(Stat, Value, n\_both\_sexes, n\_boys, n\_girls)

graph\_table2 <- ggplot(data = Table\_to\_add2, aes(x = Stat, y = num\_pos, label = Value)) +

geom\_text(size = 5) +

scale\_x\_discrete(position = "top", labels = c("both", "boys", "girls")) +

labs(y = NULL, x = NULL) +

coord\_cartesian(ylim = Ylimit) +

theme\_classic() +

theme(axis.title.x =element\_blank(),

axis.text.x = element\_text(size=14, face="bold"),

axis.line.y=element\_blank(),

axis.title.y=element\_blank(),

axis.text.y=element\_blank(),

axis.ticks.y=element\_blank())

grid.arrange(graph\_table1, graph\_table2, graph\_forest1, graph\_forest2, ncol=4, widths = c(12/100,8/100, 40/100, 40/100),

top = textGrob(paste0(group\_to\_consider, " exposure to ", molecules\_to\_consider[1], " (left plot) or ", molecules\_to\_consider[2], " (right plot) and association with ", ifelse(outcome\_to\_consider=="risk", "risk of overweight", outcome\_to\_consider)),gp=gpar(fontsize=20, face="bold")))

dev.print(png, paste0("Frigerio\_", meta\_num, molecules\_to\_consider[1], "\_", molecules\_to\_consider[2], group\_to\_consider, outcome\_to\_consider, ".png"), width=1700, height=abs(min(all\_meta\_dataiv\_specif$num\_pos\_jit))\*18+85)

}

## Creating the plots:

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c01", molecules\_to\_consider = c("PFOA", "PFOS"), outcome\_to\_consider = "BMI", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c02", molecules\_to\_consider = c("PFHxS", "PFNA"), outcome\_to\_consider = "BMI", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c03", molecules\_to\_consider = c("PFDA", "PFUA"), outcome\_to\_consider = "BMI", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c04", molecules\_to\_consider = c("PFDoA", "PFBS"), outcome\_to\_consider = "BMI", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c05", molecules\_to\_consider = c("PFOA", "PFOS"), outcome\_to\_consider = "risk", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c06", molecules\_to\_consider = c("PFHxS", "PFNA"), outcome\_to\_consider = "risk", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c07", molecules\_to\_consider = c("PFOA", "PFOS"), outcome\_to\_consider = "WC", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c08", molecules\_to\_consider = c("PFHxS", "PFNA"), outcome\_to\_consider = "WC", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c09", molecules\_to\_consider = c("PFDA", "PFUA"), outcome\_to\_consider = "WC", group\_to\_consider = "prenatal")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c10", molecules\_to\_consider = c("PFOA", "PFOS"), outcome\_to\_consider = "BMI", group\_to\_consider = "children")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c11", molecules\_to\_consider = c("PFHxS", "PFNA"), outcome\_to\_consider = "BMI", group\_to\_consider = "children")

generate\_combined\_forest\_by2(all\_meta\_data = all\_meta\_dataiv, meta\_num = "c12", molecules\_to\_consider = c("PFOA", "PFOS"), outcome\_to\_consider = "risk", group\_to\_consider = "children")

## These plots were combined and saved as Figure 2

####### End of Section 7 #######

#################### End of the script ##################