library(meta)

library(RColorBrewer)

library(dplyr)

meta\_data <- read.table(file="Meta-Datos-2.csv", header=T, sep=";", dec=".", encoding = "UTF-8")

#####Meta analisis por tipo de analgesico###############

###########################################################

res\_analisis = metagen(TE = meta\_data$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data$SEi,

studlab = meta\_data$Author.and.year,

byvar = meta\_data$Analgesic.Type,

data = meta\_data,

sm = "MD",

method.tau = "ML")

#summary(res\_analisis)

meta\_data\_sorted <- meta\_data[order(meta\_data$Analgesic.Type, meta\_data$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_sorted = metagen(TE = meta\_data\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_sorted$SEi,

studlab = meta\_data\_sorted$Author.and.year,

subgroup = meta\_data\_sorted$Analgesic.Type,

data = meta\_data\_sorted,

sm = "MD",

method.tau = "ML")

x1 <- res\_analisis\_sorted$TE.random.w

ordered\_groups <- x1[order(x1, decreasing = TRUE)]

print(ordered\_groups)

meta\_data\_sorted$Analgesic.Type <- factor(meta\_data\_sorted$Analgesic.Type, levels = names(ordered\_groups))

meta\_data\_sorted <- meta\_data\_sorted %>%

arrange(meta\_data\_sorted$Analgesic.Type)

res\_analisis\_sorted\_2 = metagen(TE = meta\_data\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_sorted$SEi,

studlab = meta\_data\_sorted$Author.and.year,

subgroup = meta\_data\_sorted$Analgesic.Type,

data = meta\_data\_sorted,

sm = "MD",

method.tau = "ML")

# Crear una paleta de colores basada en la variable$

factor\_values <- factor(meta\_data\_sorted$Line.of.Use.in.Clinics)

col\_palette <- colorRampPalette(c("#006400", "yellow", "orange", "#4D4D4D", "#777777","#B7B7B7"))(length(unique(meta\_data\_sorted$Line.of.Use.in.Clinics)))

col\_square <- col\_palette[as.numeric(factor\_values)]

tiff("forest/forest-300dpi.tiff", width=15, height=55, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_sorted\_2,

layout ="RevMan5",

slab = meta\_data\_sorted$studlab, # Etiquetas de estudios

common = FALSE,

random = TRUE,

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

#label.right = "Favours control", col.label.right = "red",

#label.left = "Favours experimental", col.label.left = "#006400",

col.square = col\_square,

col.square.lines = col\_square,

col.by = "#5B5859",

smlab = "Normalized Mean Difference",

leftcols = c("Author.and.year","NP.model", "Outcome", "Standard.analgesic", "w.random", "effect.ci"),

leftlabs = c("Analgesic Class", "NP Model", "Outcome", "Standard\nAnalgesic", "Weight", "NMD [95% CI]"),

subgroup.name = "",

fs.heading = 11,

fs.study = 10,

fs.test.overall = 10,

fs.study.label = 10,

fs.axis = 10,

fs.test.subgroup = 10,

ff.study.label = "bold",

ff.common = "plain",

ff.hetstat = "plain",

# col.diamond = "black",

# col.diamond.lines = "black",

#col.study = c("green", "blue", "red", "orange"),

# col.square = "#006400",

# col.square.lines = "black",

lwd = 1,

plotwidth="10cm",

just.addcols.left = "left",

just = "right"

)

legend("bottomleft",

horiz=TRUE,

box.lty = 1,

legend = levels(factor\_values), # Etiquetas basadas en los niveles del factor

fill = col\_palette, # Colores correspondientes

title = "Line of Use in Clinics") # Título de la leyenda

dev.off()

#####Solo medias################

tiff("forest/forest-solomedias-300dpi.tiff", width=15, height=25, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_sorted\_2,

slab = meta\_data\_sorted$studlab, # Etiquetas de estudios

overall.hetstat = TRUE,

subgroup.hetstat = TRUE,

random.subgroup = TRUE,

test.effect.subgroup.random = TRUE,

test.subgroup.random = TRUE,

test.overall.random =TRUE,

# text.random.w = "",

print.study.labels = FALSE,

study.results = FALSE,

common = FALSE,

random = TRUE,

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

leftlabs = c("Analgesic Type"),

rightlabs = c("NMD", "95% CI"),

smlab = "Normalized Mean Difference",

subgroup.name = "",

col.by = "#393D42",

col.diamond = "#00A400",

col.diamond.lines = "#393D42",

plotwidth="15cm",

xlim = c(-25,140),

at = c(-20, 0, 50, 100, 150)

)

dev.off()

############Sensitivity test###############

#########################################

# Realizar el análisis de sensibilidad con el método leave-one-out

valores\_unicos <- unique(meta\_data$nº.Paper)

print(valores\_unicos)

sensitivity\_df <- data.frame(

author = character(),

TE.common = numeric(),

seTE.common = numeric(),

statistic.common = numeric(),

pval.common = numeric(),

lower.common = numeric(),

upper.common = numeric(),

TE.random = numeric() ,

seTE.random = numeric(),

statistic.random = numeric(),

pval.random = numeric(),

method.random.ci = character(),

lower.random = numeric(),

upper.random = numeric(),

tau2 = numeric(),

se.tau2 = numeric(),

lower.tau2 = numeric(),

upper.tau2 = numeric(),

I2 = numeric(),

lower.I2 = numeric(),

upper.I2 = numeric(),

Rb = numeric(),

text.random = character(),

text.w.random = character()

)

for (num in valores\_unicos) {

author <- subset(meta\_data, nº.Paper == num)$Author.and.year

#print(author[1])

meta\_data\_filtrado <- meta\_data[meta\_data$nº.Paper != num, ]

analisis\_filtrado = metagen(TE = meta\_data\_filtrado$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_filtrado$SEi,

studlab = meta\_data\_filtrado$Author.and.year,

data = meta\_data\_filtrado,

sm = "MD",

method.tau = "ML")

sensitivity\_df <- rbind(sensitivity\_df, data.frame(

author = author[1],

TE.common = analisis\_filtrado$TE.common,

seTE.common = analisis\_filtrado$seTE.common,

statistic.common = analisis\_filtrado$statistic.common,

pval.common = analisis\_filtrado$pval.common,

lower.common = analisis\_filtrado$lower.common,

upper.common = analisis\_filtrado$upper.common,

TE.random = analisis\_filtrado$TE.random,

seTE.random = analisis\_filtrado$seTE.random,

statistic.radom = analisis\_filtrado$statistic.random,

pval.random = analisis\_filtrado$pval.random,

method.random.ci = analisis\_filtrado$method.random.ci,

lower.random = analisis\_filtrado$lower.random,

upper.random = analisis\_filtrado$upper.random,

tau2 = analisis\_filtrado$tau2,

se.tau2 = analisis\_filtrado$se.tau2,

lower.tau2 = analisis\_filtrado$lower.tau2,

upper.tau2 = analisis\_filtrado$upper.tau2,

I2 = analisis\_filtrado$I2,

lower.I2 = analisis\_filtrado$lower.I2,

upper.I2 = analisis\_filtrado$upper.I2,

Rb = analisis\_filtrado$Rb,

text.random = analisis\_filtrado$text.random,

text.w.random = analisis\_filtrado$text.w.random

))

}

# Ordenar por la columna TE (efecto del tratamiento) en orden ascendente

sensitivity\_df\_ordered <- sensitivity\_df[order(sensitivity\_df$TE.random), ]

res\_analisis\_sensitivity\_ordered = metagen(TE = sensitivity\_df\_ordered$TE.random,

seTE = sensitivity\_df\_ordered$seTE.random,

studlab = sensitivity\_df\_ordered$author,

data=sensitivity\_df\_ordered,

sm = "MD",

method.tau = "ML")

# Visualizar el forest plot del análisis de sensibilidad

tiff("forest/sensitivity.tiff", width=15, height=20, units = "in", res = 300)

forest(res\_analisis\_sensitivity\_ordered,

xlim = c(50,70),

leftcols = "studlab", # Mostrar solo los nombres de los estudios en la izquierda

rightcols = c("effect", "ci"), # Mostrar solo el efecto y el intervalo de confianza a la derecha

common = FALSE,

random = TRUE,

comb.fixed = FALSE,

comb.random = TRUE,

leftlabs = c("Omitted Study"),

rightlabs = c("NMD", "95% CI"),

smlab = "Normalized Mean Difference",

col.by = "#393D42",

col.square = "#00A400",

col.square.lines = "#393D42",

col.diamond.common = "#00A400",

col.diamond.lines = "#393D42",

plotwidth="15cm",

)

dev.off()

#####Meta analisis por tipo de Outcome###############

#####################################################

meta\_data\_sin\_NSAID <- meta\_data[!(meta\_data$Analgesic.Type %in% c("NSAID", "Mild Opioid")), ]

meta\_data\_outcome\_sorted <- meta\_data\_sin\_NSAID[order(meta\_data\_sin\_NSAID$Outcome, meta\_data\_sin\_NSAID$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_outcome\_sorted = metagen(TE = meta\_data\_outcome\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_outcome\_sorted$SEi,

studlab = meta\_data\_outcome\_sorted$Author.and.year,

byvar = meta\_data\_outcome\_sorted$Outcome,

data = meta\_data\_outcome\_sorted,

sm = "MD",

method.tau = "ML")

x\_outcome <- res\_analisis\_outcome\_sorted$TE.random.w

ordered\_groups\_outcome <- x\_outcome[order(x\_outcome, decreasing = TRUE)]

print(ordered\_groups\_outcome)

meta\_data\_outcome\_sorted$Outcome <- factor(meta\_data\_outcome\_sorted$Outcome, levels = names(ordered\_groups\_outcome))

meta\_data\_outcome\_sorted <- meta\_data\_outcome\_sorted %>%

arrange(meta\_data\_outcome\_sorted$Outcome)

res\_analisis\_outcome\_sorted = metagen(TE = meta\_data\_outcome\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_outcome\_sorted$SEi,

studlab = meta\_data\_outcome\_sorted$Author.and.year,

byvar = meta\_data\_outcome\_sorted$Outcome,

data = meta\_data\_outcome\_sorted,

sm = "MD",

method.tau = "ML")

# Crear una paleta de colores basada en la variable$

factor\_values\_outcome <- factor(meta\_data\_outcome\_sorted$Line.of.Use.in.Clinics)

col\_palette <- colorRampPalette(c("#00A400", "yellow", "orange", "#4D4D4D", "#777777","#B7B7B7"))(length(unique(meta\_data\_sorted$Line.of.Use.in.Clinics)))

col\_square <- col\_palette[as.numeric(factor\_values\_outcome)]

tiff("forest/forest-Outcome-300dpi.tiff", width=15, height=50, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_outcome\_sorted,

slab = meta\_data\_outcome\_sorted$studlab, # Etiquetas de estudios

common = FALSE,

layout ="RevMan5",

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

subgroup.name = "",

col.square = col\_square,

col.square.lines = col\_square,

col.by = "#5B5859",

smlab = "Normalized Mean Difference",

leftcols = c("Author.and.year","NP.model", "Analgesic.Type", "Standard.analgesic", "w.random", "effect.ci"),

leftlabs = c("Outcome", "NP Model", "Analgesic Type", "Standard\nAnalgesic", "Weight", "NMD [95% CI]"),

fs.heading = 11,

fs.study = 10,

fs.test.overall = 10,

fs.study.label = 10,

fs.axis = 10,

fs.test.subgroup = 10,

ff.study.label = "bold",

ff.common = "plain",

ff.hetstat = "plain",

lwd = 1,

plotwidth="10cm",

just.addcols.left = "left",

just = "right"

)

# Añadir la leyenda (una vez que el forest plot ha sido dibujado)

legend("bottomleft",

horiz=TRUE,

box.lty = 1,

legend = levels(factor\_values\_outcome), # Etiquetas basadas en los niveles del factor

fill = col\_palette, # Colores correspondientes

title = "Line of Use in Clinics") # Título de la leyenda

dev.off()

tiff("forest/forest-solomedias-outcomes-300dpi.tiff", width=15, height=15, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_outcome\_sorted,

slab = meta\_data\_outcome\_sorted$studlab, # Etiquetas de estudios

overall.hetstat = TRUE,

subgroup.hetstat = TRUE,

random.subgroup = TRUE,

test.effect.subgroup.random = TRUE,

test.subgroup.random = TRUE,

test.overall.random =TRUE,

print.study.labels = FALSE,

study.results = FALSE,

leftlabs = c("Outcome"),

rightlabs = c("NMD", "95% CI"),

smlab = "Normalized Mean Difference",

subgroup.name = "",

common = FALSE,

random = TRUE,

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

col.by = "#393D42",

col.diamond.random = "#00A400",

col.diamond.lines = "#393D42",

plotwidth="15cm",

xlim = c(-25,140),

at = c(-20, 0, 50, 100, 150)

)

dev.off()

#####Meta analisis por tipo de NP###############

#################################################

meta\_data\_NP\_sorted <- meta\_data\_sin\_NSAID[order(meta\_data\_sin\_NSAID$NP.model, meta\_data\_sin\_NSAID$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_NP\_sorted = metagen(TE = meta\_data\_NP\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_NP\_sorted$SEi,

studlab = meta\_data\_NP\_sorted$Author.and.year,

byvar = meta\_data\_NP\_sorted$NP.model,

data = meta\_data\_NP\_sorted,

sm = "MD",

method.tau = "ML")

x\_NP <- res\_analisis\_NP\_sorted$TE.random.w

ordered\_groups\_NP <- x\_NP[order(x\_NP, decreasing = TRUE)]

meta\_data\_NP\_sorted$NP.model <- factor(meta\_data\_NP\_sorted$NP.model, levels = names(ordered\_groups\_NP))

meta\_data\_NP\_sorted <- meta\_data\_NP\_sorted %>%

arrange(meta\_data\_NP\_sorted$NP.model)

res\_analisis\_NP\_sorted = metagen(TE = meta\_data\_NP\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_NP\_sorted$SEi,

studlab = meta\_data\_NP\_sorted$Author.and.year,

byvar = meta\_data\_NP\_sorted$NP.model,

data = meta\_data\_NP\_sorted,

sm = "MD",

method.tau = "ML")

# Crear una paleta de colores basada en la variable$

factor\_values\_NP <- factor(meta\_data\_NP\_sorted$Line.of.Use.in.Clinics)

col\_palette <- colorRampPalette(c("#00A400", "yellow", "orange", "#4D4D4D", "#777777","#B7B7B7"))(length(unique(meta\_data\_sorted$Line.of.Use.in.Clinics)))

col\_square <- col\_palette[as.numeric(factor\_values\_NP)]

tiff("forest/forest-NP-300dpi.tiff", width=15, height=42, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_NP\_sorted,

slab = meta\_data\_NP\_sorted$studlab, # Etiquetas de estudios

common = FALSE,

layout ="RevMan5",

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

subgroup.name = "",

col.square = col\_square,

col.square.lines = col\_square,

col.by = "#5B5859",

smlab = "Normalized Mean Difference",

leftcols = c("Author.and.year","Outcome", "Analgesic.Type", "Standard.analgesic", "w.random", "effect.ci"),

leftlabs = c("NP Model", "Outcome", "Analgesic Type", "Standard\nAnalgesic", "Weight", "NMD [95% CI]"),

fs.heading = 11,

fs.study = 10,

fs.test.overall = 10,

fs.study.label = 10,

fs.axis = 10,

fs.test.subgroup = 10,

ff.study.label = "bold",

ff.common = "plain",

ff.hetstat = "plain",

lwd = 1,

plotwidth="10cm",

just.addcols.left = "left",

just = "right"

)

# Añadir la leyenda (una vez que el forest plot ha sido dibujado)

legend("bottomleft",

horiz=TRUE,

box.lty = 1,

legend = levels(factor\_values\_NP), # Etiquetas basadas en los niveles del factor

fill = col\_palette, # Colores correspondientes

title = "Line of Use in Clinics") # Título de la leyenda

dev.off()

#####Meta analisis subset gabapentinoids###############

#######################################################

meta\_data\_subset <- meta\_data[meta\_data$Analgesic.Type == "Gabapentinoid", ]

#por modelo NP###########

meta\_data\_subset\_NP\_sorted <- meta\_data\_subset[order(meta\_data\_subset$NP.model, meta\_data\_subset$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_subset\_NP\_sorted = metagen(TE = meta\_data\_subset\_NP\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_subset\_NP\_sorted$SEi,

studlab = meta\_data\_subset\_NP\_sorted$Author.and.year,

byvar = meta\_data\_subset\_NP\_sorted$NP.model,

data = meta\_data\_subset\_NP\_sorted,

sm = "MD",

method.tau = "ML")

x\_gaba\_NP <- res\_analisis\_subset\_NP\_sorted$TE.random.w

ordered\_groups\_gaba\_NP <- x\_gaba\_NP[order(x\_gaba\_NP, decreasing = TRUE)]

meta\_data\_subset\_NP\_sorted$NP.model <- factor(meta\_data\_subset\_NP\_sorted$NP.model, levels = names(ordered\_groups\_gaba\_NP))

meta\_data\_subset\_NP\_sorted <- meta\_data\_subset\_NP\_sorted %>%

arrange(meta\_data\_subset\_NP\_sorted$NP.model)

res\_analisis\_subset\_NP\_sorted = metagen(TE = meta\_data\_subset\_NP\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_subset\_NP\_sorted$SEi,

studlab = meta\_data\_subset\_NP\_sorted$Author.and.year,

byvar = meta\_data\_subset\_NP\_sorted$NP.model,

data = meta\_data\_subset\_NP\_sorted,

sm = "MD",

method.tau = "ML")

# Crear una paleta de colores basada en la variable$

factor\_values\_subset\_NP <- factor(meta\_data\_subset\_NP\_sorted$Line.of.Use.in.Clinics)

col\_palette <- colorRampPalette(c("#00A400", "yellow", "orange", "#4D4D4D", "#777777","#B7B7B7"))(length(unique(meta\_data\_sorted$Line.of.Use.in.Clinics)))

col\_square <- col\_palette[as.numeric(factor\_values\_subset\_NP)]

tiff("forest/forest-Gabapentinoids-NP-300dpi.tiff", width=15, height=30, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_subset\_NP\_sorted,

slab = meta\_data\_subset\_NP\_sorted$studlab, # Etiquetas de estudios

common = FALSE,

layout ="RevMan5",

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

subgroup.name = "",

col.square = col\_square,

col.square.lines = col\_square,

col.by = "#5B5859",

smlab = "Normalized Mean Difference",

leftcols = c("Author.and.year","Outcome", "Standard.analgesic", "w.random", "effect.ci"),

leftlabs = c("NP Model", "Outcome", "Standard\nAnalgesic", "Weight", "NMD [95% CI]"),

fs.heading = 11,

fs.study = 10,

fs.test.overall = 10,

fs.study.label = 10,

fs.axis = 10,

fs.test.subgroup = 10,

ff.study.label = "bold",

ff.common = "plain",

ff.hetstat = "plain",

lwd = 1,

plotwidth="10cm",

just.addcols.left = "left",

just = "right"

)

# Añadir la leyenda (una vez que el forest plot ha sido dibujado)

legend("bottomleft",

horiz=TRUE,

box.lty = 1,

legend = levels(factor\_values\_subset\_NP), # Etiquetas basadas en los niveles del factor

fill = col\_palette, # Colores correspondientes

title = "Line of Use in Clinics") # Título de la leyenda

dev.off()

#por NP mode GENERIC###########

meta\_data\_subset\_NP\_Generic\_sorted <- meta\_data\_subset[order(meta\_data\_subset$NP.model.GENERIC, meta\_data\_subset$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_subset\_NP\_Generic\_sorted = metagen(TE = meta\_data\_subset\_NP\_Generic\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_subset\_NP\_Generic\_sorted$SEi,

studlab = meta\_data\_subset\_NP\_Generic\_sorted$Author.and.year,

byvar = meta\_data\_subset\_NP\_Generic\_sorted$NP.model.GENERIC,

data = meta\_data\_subset\_NP\_Generic\_sorted,

sm = "MD",

method.tau = "ML")

x\_gaba\_NP\_generic <- res\_analisis\_subset\_NP\_Generic\_sorted$TE.random.w

ordered\_groups\_gaba\_NP\_generic <- x\_gaba\_NP\_generic[order(x\_gaba\_NP\_generic, decreasing = TRUE)]

meta\_data\_subset\_NP\_Generic\_sorted$NP.model.GENERIC <- factor(meta\_data\_subset\_NP\_Generic\_sorted$NP.model.GENERIC, levels = names(ordered\_groups\_gaba\_NP\_generic))

meta\_data\_subset\_NP\_Generic\_sorted <- meta\_data\_subset\_NP\_Generic\_sorted %>%

arrange(meta\_data\_subset\_NP\_Generic\_sorted$NP.model.GENERIC)

res\_analisis\_subset\_NP\_Generic\_sorted = metagen(TE = meta\_data\_subset\_NP\_Generic\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_subset\_NP\_Generic\_sorted$SEi,

studlab = meta\_data\_subset\_NP\_Generic\_sorted$Author.and.year,

byvar = meta\_data\_subset\_NP\_Generic\_sorted$NP.model.GENERIC,

data = meta\_data\_subset\_NP\_Generic\_sorted,

sm = "MD",

method.tau = "ML")

# Crear una paleta de colores basada en la variable$

factor\_values\_subset\_NP\_generic <- factor(meta\_data\_subset\_NP\_Generic\_sorted$Line.of.Use.in.Clinics)

col\_palette <- colorRampPalette(c("#00A400", "yellow", "orange", "#4D4D4D", "#777777","#B7B7B7"))(length(unique(meta\_data\_sorted$Line.of.Use.in.Clinics)))

col\_square <- col\_palette[as.numeric(factor\_values\_subset\_NP\_generic)]

tiff("forest/forest-Gabapentinoids-NP-Generic-300dpi.tiff", width=15, height=23, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_subset\_NP\_Generic\_sorted,

slab = meta\_data\_subset\_NP\_Generic\_sorted$studlab, # Etiquetas de estudios

common = FALSE,

layout ="RevMan5",

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

subgroup.name = "",

col.square = col\_square,

col.square.lines = col\_square,

col.by = "#5B5859",

smlab = "Normalized Mean Difference",

leftcols = c("Author.and.year","Outcome", "Standard.analgesic", "w.random", "effect.ci"),

leftlabs = c("NP Model Generic", "Outcome", "Standard\nAnalgesic", "Weight", "NMD [95% CI]"),

fs.heading = 11,

fs.study = 10,

fs.test.overall = 10,

fs.study.label = 10,

fs.axis = 10,

fs.test.subgroup = 10,

ff.study.label = "bold",

ff.common = "plain",

ff.hetstat = "plain",

lwd = 1,

plotwidth="10cm",

just.addcols.left = "left",

just = "right"

)

# Añadir la leyenda (una vez que el forest plot ha sido dibujado)

legend("bottomleft",

horiz=TRUE,

box.lty = 1,

legend = levels(factor\_values\_subset\_NP\_generic), # Etiquetas basadas en los niveles del factor

fill = col\_palette, # Colores correspondientes

title = "Line of Use in Clinics") # Título de la leyenda

dev.off()

#Gabapentonoids Outcome###########################

meta\_data\_subset\_outcome\_sorted <- meta\_data\_subset[order(meta\_data\_subset$Outcome, meta\_data\_subset$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_subset\_Outcome\_sorted = metagen(TE = meta\_data\_subset\_outcome\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_subset\_outcome\_sorted$SEi,

studlab = meta\_data\_subset\_outcome\_sorted$Author.and.year,

byvar = meta\_data\_subset\_outcome\_sorted$Outcome,

data = meta\_data\_subset\_outcome\_sorted,

sm = "MD",

method.tau = "ML")

x\_gaba\_outcome <- res\_analisis\_subset\_Outcome\_sorted$TE.random.w

ordered\_groups\_gaba\_outcome <- x\_gaba\_outcome[order(x\_gaba\_outcome, decreasing = TRUE)]

meta\_data\_subset\_outcome\_sorted$Outcome <- factor(meta\_data\_subset\_outcome\_sorted$Outcome, levels = names(ordered\_groups\_gaba\_outcome))

meta\_data\_subset\_outcome\_sorted <- meta\_data\_subset\_outcome\_sorted %>%

arrange(meta\_data\_subset\_outcome\_sorted$Outcome)

res\_analisis\_subset\_Outcome\_sorted = metagen(TE = meta\_data\_subset\_outcome\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_subset\_outcome\_sorted$SEi,

studlab = meta\_data\_subset\_outcome\_sorted$Author.and.year,

byvar = meta\_data\_subset\_outcome\_sorted$Outcome,

data = meta\_data\_subset\_outcome\_sorted,

sm = "MD",

method.tau = "ML")

# Crear una paleta de colores basada en la variable$

factor\_values\_subset\_Outcome <- factor(meta\_data\_subset\_outcome\_sorted$Line.of.Use.in.Clinics)

col\_palette <- colorRampPalette(c("#00A400", "yellow", "orange", "#4D4D4D", "#777777","#B7B7B7"))(length(unique(meta\_data\_sorted$Line.of.Use.in.Clinics)))

col\_square <- col\_palette[as.numeric(factor\_values\_subset\_Outcome)]

tiff("forest/forest-Gabapentinoids-outcome-300dpi.tiff", width=15, height=28, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_subset\_Outcome\_sorted,

slab = meta\_data\_subset\_outcome\_sorted$studlab, # Etiquetas de estudios

common = FALSE,

layout ="RevMan5",

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

subgroup.name = "",

col.square = col\_square,

col.square.lines = col\_square,

col.by = "#5B5859",

smlab = "Normalized Mean Difference",

leftcols = c("Author.and.year","NP.model", "Standard.analgesic", "w.random", "effect.ci"),

leftlabs = c("Outcome", "NP model", "Standard\nAnalgesic", "Weight", "NMD [95% CI]"),

fs.heading = 11,

fs.study = 10,

fs.test.overall = 10,

fs.study.label = 10,

fs.axis = 10,

fs.test.subgroup = 10,

ff.study.label = "bold",

ff.common = "plain",

ff.hetstat = "plain",

lwd = 1,

plotwidth="10cm",

just.addcols.left = "left",

just = "right",

)

# Añadir la leyenda (una vez que el forest plot ha sido dibujado)

legend("bottomleft",

horiz=TRUE,

box.lty = 1,

legend = levels(factor\_values\_subset\_Outcome), # Etiquetas basadas en los niveles del factor

fill = col\_palette, # Colores correspondientes

title = "Line of Use in Clinics") # Título de la leyenda

dev.off()

###############NP model GENERIC################

#################################################

meta\_data\_NP\_generic\_sorted <- meta\_data\_sin\_NSAID[order(meta\_data\_sin\_NSAID$NP.model.GENERIC, meta\_data\_sin\_NSAID$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_NP\_generic\_sorted = metagen(TE = meta\_data\_NP\_generic\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_NP\_generic\_sorted$SEi,

studlab = meta\_data\_NP\_generic\_sorted$Author.and.year,

byvar = meta\_data\_NP\_generic\_sorted$NP.model.GENERIC,

data = meta\_data\_NP\_generic\_sorted,

sm = "MD",

method.tau = "ML")

x\_NP\_generic <- res\_analisis\_NP\_generic\_sorted$TE.random.w

ordered\_groups\_NP\_generic <- x\_NP\_generic[order(x\_NP\_generic, decreasing = TRUE)]

meta\_data\_NP\_generic\_sorted$NP.model.GENERIC <- factor(meta\_data\_NP\_generic\_sorted$NP.model.GENERIC, levels = names(ordered\_groups\_NP\_generic))

meta\_data\_NP\_generic\_sorted <- meta\_data\_NP\_generic\_sorted %>%

arrange(meta\_data\_NP\_generic\_sorted$NP.model.GENERIC)

res\_analisis\_NP\_generic\_sorted = metagen(TE = meta\_data\_NP\_generic\_sorted$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_NP\_generic\_sorted$SEi,

studlab = meta\_data\_NP\_generic\_sorted$Author.and.year,

byvar = meta\_data\_NP\_generic\_sorted$NP.model.GENERIC,

data = meta\_data\_NP\_generic\_sorted,

sm = "MD",

method.tau = "ML")

# Crear una paleta de colores basada en la variable$

factor\_values\_NP\_generic <- factor(meta\_data\_NP\_generic\_sorted$Line.of.Use.in.Clinics)

col\_palette <- colorRampPalette(c("#00A400", "yellow", "orange", "#4D4D4D", "#777777","#B7B7B7"))(length(unique(meta\_data\_sorted$Line.of.Use.in.Clinics)))

col\_square <- col\_palette[as.numeric(factor\_values\_NP\_generic)]

tiff("forest/forest-NP\_Generic-300dpi.tiff", width=15, height=45, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_NP\_generic\_sorted,

slab = meta\_data\_NP\_generic\_sorted$studlab, # Etiquetas de estudios

common = FALSE,

layout ="RevMan5",

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

subgroup.name = "",

col.square = col\_square,

col.square.lines = col\_square,

col.by = "#5B5859",

smlab = "Normalized Mean Difference",

leftcols = c("Author.and.year","NP.model", "Standard.analgesic", "w.random", "effect.ci"),

leftlabs = c("NP Model Generic", "NP model", "Standard\nAnalgesic", "Weight", "NMD [95% CI]"),

fs.heading = 11,

fs.study = 10,

fs.test.overall = 10,

fs.study.label = 10,

fs.axis = 10,

fs.test.subgroup = 10,

ff.study.label = "bold",

ff.common = "plain",

ff.hetstat = "plain",

lwd = 1,

plotwidth="10cm",

just.addcols.left = "left",

just = "right"

)

# Añadir la leyenda (una vez que el forest plot ha sido dibujado)

legend("bottomleft",

horiz=TRUE,

box.lty = 1,

legend = levels(factor\_values\_NP\_generic), # Etiquetas basadas en los niveles del factor

fill = col\_palette, # Colores correspondientes

title = "Line of Use in Clinics") # Título de la leyenda

dev.off()

tiff("forest/forest-solomedias-NPGeneric-300dpi.tiff", width=15, height=15, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_NP\_generic\_sorted,

slab = meta\_data\_NP\_generic\_sorted$studlab, # Etiquetas de estudios

overall.hetstat = TRUE,

subgroup.hetstat = TRUE,

random.subgroup = TRUE,

test.effect.subgroup.random = TRUE,

test.subgroup.random = TRUE,

test.overall.random =TRUE,

print.study.labels = FALSE,

study.results = FALSE,

leftlabs = c("NP Model Generic"),

rightlabs = c("NMD", "95% CI"),

smlab = "Normalized Mean Difference",

subgroup.name = "",

common = FALSE,

random = TRUE,

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

col.by = "#393D42",

col.diamond.random = "#00A400",

col.diamond.lines = "#393D42",

plotwidth="15cm",

xlim = c(-25,140),

at = c(-20, 0, 50, 100, 150)

)

dev.off()

###################Gabapentin vs Pregabalin##############

#########################################################

meta\_data\_subset\_analgesic <- meta\_data[meta\_data$Standard.analgesic %in% c("Gabapentin","Pregabalin"), ]

meta\_data\_subset\_analgesic <- meta\_data\_subset\_analgesic[order(meta\_data\_subset\_analgesic$Standard.analgesic, meta\_data\_subset\_analgesic$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_subset\_analgesic = metagen(TE = meta\_data\_subset\_analgesic$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_subset\_analgesic$SEi,

studlab = meta\_data\_subset\_analgesic$Author.and.year,

byvar = meta\_data\_subset\_analgesic$Standard.analgesic,

data = meta\_data\_subset\_analgesic,

sm = "MD",

method.tau = "ML")

# Crear una paleta de colores basada en la variable$

factor\_values\_analgesic <- factor(meta\_data\_subset\_analgesic$Line.of.Use.in.Clinics)

col\_palette <- colorRampPalette(c("#00A400", "yellow", "orange", "#4D4D4D", "#777777","#B7B7B7"))(length(unique(meta\_data\_sorted$Line.of.Use.in.Clinics)))

col\_square <- col\_palette[as.numeric(factor\_values\_analgesic)]

tiff("forest/forest-GabvsPre-300dpi.tiff", width=15, height=22, units = "in", res = 300) # Tamaño A4 en pulgadas, 300 DPI

plot.new()

# Crear el forest plot

forest(res\_analisis\_subset\_analgesic,

slab = meta\_data\_subset\_analgesic$studlab, # Etiquetas de estudios

common = FALSE,

layout ="RevMan5",

comb.fixed = FALSE,

comb.random = TRUE,

prediction = TRUE,

test.effect.subgroup.random = TRUE,

test.subgroup.random = TRUE,

test.overall.random =TRUE,

subgroup.name = "",

col.square = col\_square,

col.square.lines = col\_square,

col.by = "#5B5859",

smlab = "Normalized Mean Difference",

leftcols = c("Author.and.year","NP.model", "Outcome", "w.random", "effect.ci"),

leftlabs = c("Standard Analgesic", "NP model", "Outcome", "Weight", "NMD [95% CI]"),

fs.heading = 11,

fs.study = 10,

fs.test.overall = 10,

fs.study.label = 10,

fs.axis = 10,

fs.test.subgroup = 10,

ff.study.label = "bold",

ff.common = "plain",

ff.hetstat = "plain",

lwd = 1,

plotwidth="10cm",

just.addcols.left = "left",

just = "right"

)

# Añadir la leyenda (una vez que el forest plot ha sido dibujado)

legend("bottomleft",

horiz=TRUE,

box.lty = 1,

legend = levels(factor\_values\_analgesic), # Etiquetas basadas en los niveles del factor

fill = col\_palette, # Colores correspondientes

title = "Line of Use in Clinics") # Título de la leyenda

dev.off()

#####Meta analisis por sexo###############

#########################################

meta\_data\_sorted\_sex <- meta\_data[order(meta\_data$Sex, meta\_data$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_sorted\_sex = metagen(TE = meta\_data\_sorted\_sex$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_sorted\_sex$SEi,

studlab = meta\_data\_sorted\_sex$Author.and.year,

subgroup = meta\_data\_sorted\_sex$Sex,

data = meta\_data\_sorted\_sex,

sm = "MD",

method.tau = "ML")

reg\_summary\_sex <- capture.output(summary(res\_analisis\_sorted\_sex))

writeLines(reg\_summary\_sex, con = "analisis/meta-analisis-por-sexo.txt")

#####Meta analisis por Especie###############

################################################

meta\_data\_sorted\_Specie <- meta\_data[order(meta\_data$Specie, meta\_data$ESi.Normalised.mean.difference..NMD.), ]

res\_analisis\_sorted\_Specie = metagen(TE = meta\_data\_sorted\_Specie$ESi.Normalised.mean.difference..NMD. ,

seTE = meta\_data\_sorted\_Specie$SEi,

studlab = meta\_data\_sorted\_Specie$Author.and.year,

subgroup = meta\_data\_sorted\_Specie$Specie,

data = meta\_data\_sorted\_Specie,

sm = "MD",

method.tau = "ML")

reg\_summary\_specie <- capture.output(summary(res\_analisis\_sorted\_Specie))

writeLines(reg\_summary\_specie, con = "analisis/meta-analisis-por-specie.txt")