```
library(readxl)
library(netmeta)
library(WriteXLS)
library(tidyverse)
library(dplyr)

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

data <- read_excel("~/Documents/Research/Active Projects/BD NMA Adjunctive/BD NMA
Adjuncts.xlsx",
                   sheet = "Modified Analysis")
attach(data)
data <- as.data.frame(data)
attach(data)

#demographics
table(Year)
table(Country)
table(Agents)
table(Class)
length(Class)
table(Subtype)
table(Study[Subtype=="BP-II"])
sum(N)
sum((N_2)[Treatment_2=="Placebo"])
sum(N)-sum((N_2)[Treatment_2=="Placebo"])
summary(Age)
sd(Age)
sum(F1,F2,F3,F4)

#duration
summary(Weeks)

#arms
table(Study[Arms>2])

#quality
table(Overall_ROB)

##############################################################
# Transform data from arm-based format to contrast-based fRRmat
## Outcome: response
p1 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Responders_1, Responders_2, Responders_3, Responders_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: remission
p2 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Remitters_1, Remitters_2, Remitters_3, Remitters_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: completion
p3 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Completed_1, Completed_2, Completed_3, Completed_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: dropouts (all-cause)
```

```
p4 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Dropouts_1, Dropouts_2, Dropouts_3, Dropouts_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

## Outcome: discontinuation due to adverse events
p5 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(AE_1, AE_2, AE_3, AE_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

## Outcome: mania
p6 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Mania_1, Mania_2, Mania_3, Mania_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

## Outcome: symptom improvement (difference)
p7 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               mean = list(End_1, End_2, End_3, End_4),
               sd = list(End_SD_1, End_SD_2, End_SD_3, End_SD_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "SMD")

##############################################
# Conduct random effects network meta-analysis
## Outcome: response
net1 <- netmeta(p1, comb.fixed = FALSE, reference = "Placebo")
print(summary(net1), digits = 2)

##  Outcome: remission
net2 <- netmeta(p2, comb.fixed = FALSE, reference = "Placebo")
print(summary(net2), digits = 2)

##  Outcome: completion
net3 <- netmeta(p3, comb.fixed = FALSE, reference = "Placebo")
print(summary(net3), digits = 2)

##  Outcome: dropouts (all-cause)
net4 <- netmeta(p4, comb.fixed = FALSE, reference = "Placebo")
print(summary(net4), digits = 2)

## Outcome: discontinuation due to adverse events
net5 <- netmeta(p5, comb.fixed = FALSE, reference = "Placebo")
print(summary(net5), digits = 2)

## Outcome: mania
net6 <- netmeta(p6, comb.fixed = FALSE, reference = "Placebo")
print(summary(net6), digits = 2)

## Outcome: symptom improvement (depression)
net7 <- netmeta(p7, comb.fixed = FALSE, reference = "Placebo", tol.multiarm = 1)
print(summary(net7), digits = 2)

#####################################
# Network graph with default settings
netgraph(net1, offset = 0.02, cex = 0.55) #response
netgraph(net2) #remission
```

```
netgraph(net3) #completion
netgraph(net4) #dropout (all)
netgraph(net5) #dropout (ae)
netgraph(net6) #mania
netgraph(net7) #symptoms

######################
# Network forest plots
forest(net1, ref="Placebo", xlab="RR for response",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")

forest(net2, ref="Placebo", xlab="RR for remission",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")

forest(net3, ref="Placebo", xlab="RR for completion",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")

forest(net4, ref="Placebo", xlab="RR for all drop outs",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net5, reference.group="Placebo", xlab="RR for dropouts due to adverse events",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net6, ref="Placebo", xlab="RR for mania",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net7, ref="Placebo", xlab="SMD for depression severity change",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

###############
# decomposition
decomp.design(net1) #response
decomp.design(net2) #remission
decomp.design(net3) #completion
decomp.design(net4) #dropout (all)
decomp.design(net5) #dropout (ae)
decomp.design(net6) #mania
decomp.design(net7) #symptoms

##############
# Funnel plots
funnel(net1, order = net1$trts, linreg = TRUE, digits.pval = 2,
       legend = FALSE, col = "purple", xlab = "RR for response")

funnel(net2, order = net2$trts, linreg = TRUE, digits.pval = 2,
```

```
       legend = FALSE, col = "blue", xlab = "RR for remission")

funnel(net3, order = net3$trts, linreg = TRUE, digits.pval = 2,
       legend = FALSE, col = "red", xlab = "RR for completion")

funnel(net4, order = net4$trts, linreg = TRUE, digits.pval = 2,
       legend = FALSE, col = "green", xlab = "RR for dropouts")

funnel(net5, order = net5$trts, linreg = TRUE, digits.pval = 2,
       legend = FALSE, col = "yellow", xlab = "RR for dropouts due to adverse events")

funnel(net6, order = net6$trts, linreg = TRUE, digits.pval = 2,
       legend = FALSE, col = "orange", xlab = "RR for mania")

funnel(net7, order = net7$trts, linreg = TRUE, digits.pval = 2,
       legend = FALSE, col = "brown", xlab = "SMD for depression symptoms")

##################################################################################
# League tables

league1 <- netleague(net1, comb.fixed = FALSE, digits = 2, seq = netrank(net1))
WriteXLS(league1$random, ExcelFileName = "league_response.xls",
         SheetNames = "response", col.names = FALSE)

league2 <- netleague(net2, comb.fixed = FALSE, digits = 2, seq = netrank(net2))
WriteXLS(league2$random, ExcelFileName = "league_remission.xls",
         SheetNames = "remission", col.names = FALSE)

league3 <- netleague(net3, comb.fixed = FALSE, digits = 2, seq = netrank(net3))
WriteXLS(league3$random, ExcelFileName = "league_completion.xls",
         SheetNames = "completion", col.names = FALSE)

league4 <- netleague(net4, comb.fixed = FALSE, digits = 2, seq = netrank(net4))
WriteXLS(league4$random, ExcelFileName = "league_loss.xls",
         SheetNames = "loss", col.names = FALSE)

league5 <- netleague(net5, comb.fixed = FALSE, digits = 2, seq = netrank(net5))
WriteXLS(league5$random, ExcelFileName = "league_ae.xls",
         SheetNames = "ae", col.names = FALSE)

league6 <- netleague(net6, comb.fixed = FALSE, digits = 2, seq = netrank(net6))
WriteXLS(league6$random, ExcelFileName = "league_mania.xls",
         SheetNames = "mania", col.names = FALSE)

league7 <- netleague(net7, comb.fixed = FALSE, digits = 2, seq = netrank(net7))
WriteXLS(league7$random, ExcelFileName = "league_depression_severity.xls",
         SheetNames = "severity", col.names = FALSE)

##############################################################################
##############################################################################
##############################################################################
library(readxl)
library(netmeta)
library(WriteXLS)
library(tidyverse)
library(dplyr)

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

data <- read_excel("~/Documents/Research/Active Projects/BD NMA Adjunctive/BD NMA
Adjuncts.xlsx",
                   sheet = "Modified Analysis")
attach(data)

table(Subtype)
```

```
#filter: BP-I
data <-
  data %>%
  filter(Subtype == 'BP-I')
attach(data)

####pairwise
p1 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Responders_1, Responders_2, Responders_3, Responders_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: remission
p2 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Remitters_1, Remitters_2, Remitters_3, Remitters_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: completion
p3 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Completed_1, Completed_2, Completed_3, Completed_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: dropouts (all-cause)
p4 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Dropouts_1, Dropouts_2, Dropouts_3, Dropouts_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

## Outcome: discontinuation due to adverse events
p5 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(AE_1, AE_2, AE_3, AE_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

## Outcome: mania
p6 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Mania_1, Mania_2, Mania_3, Mania_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

## Outcome: symptom improvement (difference)
p7 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               mean = list(End_1, End_2, End_3, End_4),
               sd = list(End_SD_1, End_SD_2, End_SD_3, End_SD_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "SMD")

# Conduct random effects network meta-analysis
## Outcome: response
net1 <- netmeta(p1, comb.fixed = FALSE, reference = "Placebo")
```

```
print(summary(net1), digits = 2)

##  Outcome: remission
net2 <- netmeta(p2, comb.fixed = FALSE, reference = "Placebo")
print(summary(net2), digits = 2)

##  Outcome: completion
net3 <- netmeta(p3, comb.fixed = FALSE, reference = "Placebo")
print(summary(net3), digits = 2)

##  Outcome: dropouts (all-cause)
net4 <- netmeta(p4, comb.fixed = FALSE, reference = "Placebo")
print(summary(net4), digits = 2)

## Outcome: discontinuation due to adverse events
net5 <- netmeta(p5, comb.fixed = FALSE, reference = "Placebo")
print(summary(net5), digits = 2)

## Outcome: mania
net6 <- netmeta(p6, comb.fixed = FALSE, reference = "Placebo")
print(summary(net6), digits = 2)

## Outcome: symptom improvement (depression)
net7 <- netmeta(p7, comb.fixed = FALSE, reference = "Placebo", tol.multiarm = 1)
print(summary(net7), digits = 2)

# Network forest plots
forest(net1, ref="Placebo", xlab="RR for response",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")

forest(net2, ref="Placebo", xlab="RR for remission",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")

forest(net3, ref="Placebo", xlab="RR for completion",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")

forest(net4, ref="Placebo", xlab="RR for all drop outs",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net5, reference.group="Placebo", xlab="RR for dropouts due to adverse events",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net6, ref="Placebo", xlab="RR for mania",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net7, ref="Placebo", xlab="SMD for depression severity change",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
```

```
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

##############################################################################
##############################################################################
##############################################################################
library(readxl)
library(netmeta)
library(WriteXLS)
library(tidyverse)
library(dplyr)

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

data <- read_excel("~/Documents/Research/Active Projects/BD NMA Adjunctive/BD NMA
Adjuncts.xlsx",
                   sheet = "Modified Analysis")
attach(data)

table(MS)

#filter: MS
data <-
  data %>%
  filter(MS == 'Antipsychotic')
attach(data)

####pairwise
p1 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Responders_1, Responders_2, Responders_3, Responders_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: remission
p2 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Remitters_1, Remitters_2, Remitters_3, Remitters_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: completion
p3 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Completed_1, Completed_2, Completed_3, Completed_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

##  Outcome: dropouts (all-cause)
p4 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Dropouts_1, Dropouts_2, Dropouts_3, Dropouts_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

## Outcome: discontinuation due to adverse events
p5 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(AE_1, AE_2, AE_3, AE_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")
```

```
## Outcome: mania
p6 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               event = list(Mania_1, Mania_2, Mania_3, Mania_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "RR")

## Outcome: symptom improvement (difference)
p7 <- pairwise(treat = list(Class_1, Class_2, Class_3, Class_4),
               mean = list(End_1, End_2, End_3, End_4),
               sd = list(End_SD_1, End_SD_2, End_SD_3, End_SD_4),
               n = list(N_1, N_2, N_3, N_4),
               studlab = Study,
               data = data,
               sm = "SMD")

# Conduct random effects network meta-analysis
## Outcome: response
net1 <- netmeta(p1, comb.fixed = FALSE, reference = "Placebo")
print(summary(net1), digits = 2)

##  Outcome: remission
net2 <- netmeta(p2, comb.fixed = FALSE, reference = "Placebo")
print(summary(net2), digits = 2)

##  Outcome: completion
net3 <- netmeta(p3, comb.fixed = FALSE, reference = "Placebo")
print(summary(net3), digits = 2)

##  Outcome: dropouts (all-cause)
net4 <- netmeta(p4, comb.fixed = FALSE, reference = "Placebo")
print(summary(net4), digits = 2)

## Outcome: discontinuation due to adverse events
net5 <- netmeta(p5, comb.fixed = FALSE, reference = "Placebo")
print(summary(net5), digits = 2)

## Outcome: mania
net6 <- netmeta(p6, comb.fixed = FALSE, reference = "Placebo")
print(summary(net6), digits = 2)

## Outcome: symptom improvement (depression)
net7 <- netmeta(p7, comb.fixed = FALSE, reference = "Placebo", tol.multiarm = 1)
print(summary(net7), digits = 2)

# Network forest plots
forest(net1, ref="Placebo", xlab="RR for response",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")

forest(net2, ref="Placebo", xlab="RR for remission",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")

forest(net3, ref="Placebo", xlab="RR for completion",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-TE, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors placebo", label.right = "Favors drug")
```

```
forest(net4, ref="Placebo", xlab="RR for all drop outs",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net5, reference.group="Placebo", xlab="RR for dropouts due to adverse events",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net6, ref="Placebo", xlab="RR for mania",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")

forest(net7, ref="Placebo", xlab="SMD for depression severity change",
       rightcols=c("effect", "ci", "Pscore"), rightlabs="P-Score", leftcols=c("studlab", "k"),
       leftlabs=c("Contrast\nto Placebo", "Direct\nComparisons"), just.addcols="right",
       sortvar=-Pscore, smlab = "Random Effects Model", drop.reference.group = TRUE,
       label.left = "Favors drug", label.right = "Favors placebo")
```