

```
#####  
# LOAD PACKAGES  
#####  
install.packages("meta")  
library(meta)  
  
###labels  
install.packages("expss")  
library("expss")  
  
setwd("~/Sepsis_Review/Analyse")  
  
#####  
## READ DATA  
#####  
library(readxl)  
Neonates<- read_excel("C:/Users/ReichertF/Documents/Sepsis_Review/Analyse/  
Neonates_Analysetab_2020_01_09.xlsx")  
  
#####  
## DATA PREP  
#####  
###Subset of studies of 1st SR  
Test<- subset(Neonates, Test==1)  
  
###by sepsis type  
###Label type_sepsis: 1 EOS; 2 LOS; 3 mixed  
EOS<- subset(Neonates,(type_sepsis==1 & subgroup==0))  
LOS<- subset(Neonates,(type_sepsis==2 & subgroup==0))  
mixed<- subset(Neonates,(type_sepsis==3 & subgroup==0))  
all<- subset(Neonates,subgroup==0)  
all$type_sepsis<-factor(all$type_sepsis, levels = c(1,2,3), labels =  
c("EOS","LOS","EOS & LOS"))  
  
###by subgroup  
###Label subgroup: 0 none 1 NBW; 2 LBW ; 3 VLBW; 4 preterm; 5 term; 9 LBW  
(incl.VLBW)  
mixed_subgroup<- subset(Neonates,(type_sepsis==3 & subgroup!=0))  
#subgroups (GA+BW), no study with subgroup "9"  
EOS_subgroup<- subset(Neonates,(type_sepsis==1 & subgroup!=0 & subgroup!=9))  
#subgroups (GA+BW), without overlapping definition for LBW ("9")  
LOS_subgroup<- subset(Neonates,(type_sepsis==2 & subgroup!=0 & subgroup!=9))  
#subgroups (GA+BW), without overlapping definition for LBW ("9")  
#mixed_GA<- subset(Neonates,(type_sepsis==3 & (subgroup==4 | subgroup==5)))  
#by gestational age  
#EOS_GA<- subset(Neonates,(type_sepsis==1 & (subgroup==4 | subgroup==5)))  
#by gestational age  
#mixed_GG<- subset(Neonates,(type_sepsis==3 & (subgroup==1 | subgroup==2 |  
subgroup==3))) #by birth weight  
#EOS_GG<- subset(Neonates,(type_sepsis==1 & (subgroup==1 | subgroup==2 |  
subgroup==3))) #by birth weight  
#mixed_GGrisk<- subset(Neonates,(type_sepsis==3 & (subgroup==2 | subgroup==3)))  
#only risk groups birth weight  
#EOS_GGrisk<- subset(Neonates,(type_sepsis==1 & (subgroup==2 | subgroup==3)))  
#only risk groups birth weight  
#mixed_all<- subset(Neonates,type_sepsis==3)
```

```
EOS$decade[EOS$year_from >=1989 & EOS$year_from<=1998]<-2
EOS$decade[EOS$year_from >=1999 & EOS$year_from<=2008]<-3
EOS$decade[EOS$year_from >=2009]<-4
EOS$decade <- factor(EOS$decade, levels = c(1,2,3,4), labels = c("Before 1989",
"1989-1998", "1999-2008", "2009-2018"))

LOS$decade<-9
LOS$decade[LOS$year_from <=1988]<-1
LOS$decade[LOS$year_from >=1989 & LOS$year_from<=1998]<-2
LOS$decade[LOS$year_from >=1999 & LOS$year_from<=2008]<-3
LOS$decade[LOS$year_from >=2009]<-4
LOS$decade <- factor(LOS$decade, levels = c(1,2,3,4), labels = c("Before 1989",
"1989-1998", "1999-2008", "2009-2018"))

mixed$decade<-9
mixed$decade[mixed$year_from <=1988]<-1
mixed$decade[mixed$year_from >=1989 & mixed$year_from<=1998]<-2
mixed$decade[mixed$author == "Kaushik"]<-2 #Kaushik: Publikation 1998
mixed$decade[mixed$year_from >=1999 & mixed$year_from<=2008]<-3
mixed$decade[mixed$year_from >=2009]<-4
mixed$decade <- factor(mixed$decade, levels = c(1,2,3,4), labels = c("Before
1989", "1989-1998", "1999-2008", "2009-2018"))

### by setting: 0 community; 1 hospital
mixed$setting<- factor(mixed$setting, levels = c(0,1), labels = c("Community",
"Hospital"))
var_lab(mixed$setting) = "Study setting"
EOS$setting<- factor(EOS$setting, levels = c(0,1), labels = c("Community",
"Hospital"))

### by WHO region
###Label: 1=African Region, 2=Region of the Americas, 3=South-East Asia Region,
4= European Region,5= Eastern Mediterranean Region, 6=Western Pacific Region
mixed$Region<- factor(mixed$WHO_region, levels = c(1,2,3,4,5,6), labels =
c("AFR", "PAR", "SEAR", "EUR", "EMR", "WPR"))
EOS$Region<- factor(EOS$WHO_region, levels = c(1,2,3,4,5,6), labels = c("AFR",
"PAR", "SEAR", "EUR", "EMR", "WPR"))

### by income
###Label: 1=low 3=middle 4=high
mixed$Income_Group<- factor(mixed$income2, levels = c(1,3,4), labels = c("Low
Income", "Middle Income", "High Income"))
EOS$Income_Group<- factor(EOS$income2, levels = c(1,3,4), labels = c("Low
Income", "Middle Income", "High Income"))

#=====
## meta-analysis, Incidence
#=====
###Test - reproducton of results of previous SR
Carolin<-
metaprop(n_sepsis_calc,n_livebirths,studlab=paste(author,year_from),method.tau="S.
= "inverse",data=Test,pscale = 100000)
forest(Carolin,leftcols=c("studlab"),rightcols=c("effect",
"ci"),pscale=100000,hetstat=F,comb.fixed=F,rightlabs=c("Incidence","95% CI"))
....
```

```
### time
####mixed
metamixed_decades<-
metaprop(n_sepsis_calc,n_livebirths,studlab=paste(author,year_from,"-",year_to),m
= "inverse",data=mixed,pscale = 100000,byvar = decade)
forest(metamixed_decades,leftcols=c("studlab"),leftlabs=c("Study and observation
period"),smlab="Cases per 100 000 livebirths",print.byvar=FALSE,
      rightcols=c("effect",
"ci"),xlim=c(0,20000),pscale=100000,hetstat=T,comb.fixed=F,rightlabs=c("Incidence
CI"))
####EOS
metaEOS_decades<-
metaprop(n_sepsis_calc,n_livebirths,studlab=paste(author,year_from,"-",year_to),m
= "inverse",data=EOS,pscale = 100000,byvar = decade)
forest(metaEOS_decades,leftcols=c("studlab"),leftlabs=c("Study and observation
period"),smlab="Cases per 100 000 livebirths",print.byvar=FALSE,
      rightcols=c("effect",
"ci"),xlim=c(0,20000),pscale=100000,hetstat=T,comb.fixed=F,rightlabs=c("Incidence
CI"))
####LOS
metaLOS_decades<-
metaprop(n_sepsis_calc,n_livebirths,studlab=paste(author,year_from,"-",year_to),m
= "inverse",data=LOS,pscale = 100000,byvar = decade)
forest(metaLOS_decades,leftcols=c("studlab"),leftlabs=c("Study and observation
period"),smlab="Cases per 100 000 livebirths",print.byvar=FALSE,
      rightcols=c("effect",
"ci"),xlim=c(0,20000),pscale=100000,hetstat=T,comb.fixed=F,rightlabs=c("Incidence
CI"))

###setting
####mixed
metamixed_setting<-
metaprop(n_sepsis_calc,n_livebirths,studlab=paste(author,"|",year_from,"-",year_to)
= "inverse",data=mixed,pscale = 100000,byvar = setting)
forest(metamixed_setting,leftcols=c("studlab"),leftlabs=c("Study and observation
period"),
      colgap.forest.left="1cm",smlab="Cases per 100 000 livebirths",
      print.byvar = F,rightcols=c("effect",
"ci"),xlim=c(0,20000),pscale=100000,hetstat=T,comb.fixed=F,rightlabs=c("Incidence
CI"))
####EOS
metaEOS_setting<-
metaprop(n_sepsis_calc,n_livebirths,studlab=paste(author,"|",year_from,"-",year_to)
= "inverse",data=EOS,pscale = 100000,byvar = setting)
forest(metaEOS_setting,leftcols=c("studlab"),leftlabs=c("Study and observation
period"),colgap.forest.left="1cm",smlab="Cases per 100 000
livebirths",print.byvar = F,rightcols=c("effect",
"ci"),xlim=c(0,50000),pscale=100000,hetstat=T,comb.fixed=F,rightlabs=c("Incidence
CI"))

####WHOregions
####mixed
metamixed_WHO<-
metaprop(n_sepsis_calc,n_livebirths,studlab=paste(author,"|",year_from,"-",year_to)
= "inverse",data=mixed,pscale = 100000,byvar = Region)
forest(metamixed_WHO,leftcols=c("studlab", "country", "setting"),leftlabs=c("Study
```

```
#forest (metamixed_GGrisk, leftcols=c("studlab"), rightcols=c("effect",
"ci"), xlim=c(0,50000), pscale=100000, hetstat=T, print.Q=T, comb.fixed=F, rightlabs=c('
CI"), colgap.forest.left = "60mm")
#metaEOS_GGrisk<-
metaprop(n_sepsis_calc, n_livebirths, studlab=paste(author, "|", year_from, "-", year_to
= "inverse", data=EOS_GGrisk, pscale = 100000, byvar = Birthweight)
#forest (metaEOS_GGrisk, leftcols=c("studlab"), leftlabs=c("Study and observation
period"), smlab="Cases per 100 000 livebirths",
# print.byvar=FALSE, rightcols=c("effect",
"ci"), xlim=c(0,50000), pscale=100000, hetstat=T, print.Q=T, comb.fixed=F, rightlabs=c('
CI"), colgap.forest.left = "60mm")

#=====
## mortality
#=====
all_mort<-subset(all, n_deaths>0)
all_mort$n_deaths<-as.integer(all_mort$n_deaths)
metaall_mort<-
metaprop(n_deaths, n_mort_denom, studlab=paste(author, "|", year_from, "-", year_to), me
= "inverse", data=all_mort, pscale = 100, byvar = type_sepsis)
forest(metaall_mort, leftcols=c("studlab", "n_deaths", "n_mort_denom"), leftlabs=c("S
and observation period", "Deceased cases", "Sepsis
cases"), digits.addcols.left=0, just.addcols.left = c("right"),
colgap.forest.left="1cm", smlab="Deaths per 100 sepsis cases",
print.byvar=FALSE, rightcols=c("effect",
"ci"), xlim=c(0,100), pscale=100, hetstat=T, comb.fixed=F, rightlabs=c("Mortality
(%)", "95% CI"), overall = F, overall.hetstat = FALSE,)

#=====
## culture positivity
#=====
library(readxl)
#xblood_all1x <- read_excel("C:/Users/ReichertF/Documents/Sepsis_Review/NEONATES_
Pathogens_Resistances.xlsx", sheet = "all (1x)")
blood <- read_excel("C:/Users/ReichertF/Documents/Sepsis_Review/NEONATES_
Pathogens_Resistances.xlsx", sheet = "EOS+LOS BK")
#xblood_all1x = as.data.frame(blood_all1x)
blood = as.data.frame(blood)
blood$type_sspsis<-factor(blood$type_sspsis, levels = c(1,2,3), labels =
c("EOS", "LOS", "EOS & LOS"))

###by sepsis type
metablood<-
metaprop(n_culture_pos, n_culture, studlab=paste(Author), method.tau="SJ", method =
"inverse", data=blood, pscale = 100, byvar = type_sspsis)
forest(metablood,
leftcols=c("studlab", "n_culture_pos", "n_culture"), leftlabs=c("Study",
"Positive blood cultures", "Sepsis
cases"), digits.addcols.left=0, just.addcols.left = c("right"),
colgap.forest.left="1cm", smlab="Proportion of positive blood cultures",
print.byvar=FALSE, rightcols=c("effect",
"ci"), xlim=c(0,100), pscale=100, hetstat=T, comb.fixed=F, rightlabs=c("(%)", "95%
CI"), overall = F, overall.hetstat = FALSE,)

###overall
#xmetablood_all1x<-
```