**BAYESIAN meta-analysis**

library(brms)

**MORTALITY**

PRIORS

priors <- c(prior(normal(0,1000), class = Intercept),

prior(cauchy(0,0.5), class = sd))

META-ANALYSIS Log RR

m.brm <- brm(TE|se(seTE) ~ 1 + (1|Author),

data = mort,

prior = priors,

iter = 10000)

summary(m.brm)

pp\_check(m.brm)

ranef(m.brm)

post.samples <- posterior\_samples(m.brm, c("^b", "^sd"))

names(post.samples)

names(post.samples) <- c("logRR", "tau")

PLOT POSTERIOR DISTRIBUTION TE

ggplot(aes(x = logRR), data = post.samples) +

geom\_density(fill = "lightblue",

color = "lightblue", alpha = 0.7) +

geom\_point(y = 0,

x = mean(post.samples$logRR)) +

labs(x = expression(italic(logRR)),

y = element\_blank()) +

theme\_minimal()

PLOT POSTERIOR DISTRIBUTION TAU

ggplot(aes(x = tau), data = post.samples) +

geom\_density(fill = "lightgreen",

color = "lightgreen", alpha = 0.7) +

geom\_point(y = 0,

x = mean(post.samples$tau)) +

labs(x = expression(tau),

y = element\_blank()) +

theme\_minimal()

POSTERIOR DISTRIBUTION

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.0953)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.1823)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.2624)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.3365)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.4055)

library(tidybayes)

library(dplyr)

library(ggplot2)

library(ggridges)

library(glue)

library(stringr)

library(forcats)

library(ggpubr)

study.draws <- spread\_draws(m.brm, r\_Author[Author,], b\_Intercept) %>%

mutate(b\_Intercept = r\_Author + b\_Intercept, type = "Study-level Estimate")

pooled.effect.draws <- spread\_draws(m.brm, b\_Intercept) %>%

mutate(Author = "Pooled Effect", type = "Pooled Estimate")

fp\_data <- bind\_rows(study.draws, pooled.effect.draws) %>%

ungroup() %>%

mutate(b\_Intercept = b\_Intercept %>% exp) %>%

mutate(Author = str\_replace\_all(Author, "[.]", " ")) %>%

mutate(Author = reorder(Author, b\_Intercept))

#Create title and subtitles for the plot

main\_title <- "5-year all-cause mortality"

subtitle <- "non-informative prior"

#Plot

ggplot(data = fp\_data,

aes(y = relevel(Author, "Pooled Effect"),

x = b\_Intercept,

fill = type

)) +

#Add Density plots

geom\_density\_ridges(col = NA,

scale = 0.9, #Slightly decrease size so it fits

alpha = 0.7,

) +

geom\_vline(xintercept = 1, color = "black",

lwd = 1, linetype = 2) +

stat\_halfeye(alpha = 0.7, .width = 0.95) +

#Set colors

scale\_fill\_manual(values = c("salmon", "lightblue")) +

#Create title

ggtitle(main\_title,

subtitle = subtitle) +

#X and Y axes aesthetics

scale\_y\_discrete(name = "Study") +

scale\_x\_continuous(name = "Relative Risk",

trans = "log",

breaks = c(0.5, 1, 2)) +

#Set reasonable Y axis limits

coord\_cartesian(xlim = c(0.5, 2)) +

#Set theme

theme\_pubclean() +

theme(text = element\_text(size = 23),

plot.title=element\_text(face = "bold",hjust = 0.0, size = 18),

plot.subtitle = element\_text(face = "bold", size = 15, hjust = 0.0, color = "grey45"),

axis.text.x = element\_text(size = 20, face = "bold"),

axis.text.y = element\_text(size = 15, face = "bold"),

axis.title.x = element\_text(size = 25, face = "bold"),

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

axis.line = element\_line(colour = "black", linewidth = 1.2),

plot.margin = margin(0.5, 1, 0.5, 1, "cm"),

legend.background = element\_rect(fill = "transparent"),

legend.position = "none",

legend.text = element\_text(size = 12, face = "bold"),

legend.key.width = unit(1.5, "cm"),

legend.key.height = unit(0.75, "cm"))

**STROKE**

PRIORS

priors <- c(prior(normal(0,2), class = Intercept),

prior(cauchy(0,0.5), class = sd))

META-ANALYSIS Log RR

m.brm <- brm(TE|se(seTE) ~ 1 + (1|Author),

data = stroke,

prior = priors,

iter = 10000)

summary(m.brm)

pp\_check(m.brm)

ranef(m.brm)

post.samples <- posterior\_samples(m.brm, c("^b", "^sd"))

names(post.samples)

names(post.samples) <- c("logRR", "tau")

PLOT POSTERIOR DISTRIBUTION TE

ggplot(aes(x = logRR), data = post.samples) +

geom\_density(fill = "lightblue",

color = "lightblue", alpha = 0.7) +

geom\_point(y = 0,

x = mean(post.samples$logRR)) +

labs(x = expression(italic(logRR)),

y = element\_blank()) +

theme\_minimal()

PLOT POSTERIOR DISTRIBUTION TAU

ggplot(aes(x = tau), data = post.samples) +

geom\_density(fill = "lightgreen",

color = "lightgreen", alpha = 0.7) +

geom\_point(y = 0,

x = mean(post.samples$tau)) +

labs(x = expression(tau),

y = element\_blank()) +

theme\_minimal()

POSTERIOR DISTRIBUTION

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(-0.3255)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(-0.8109)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(-1.7917)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf()

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf()

library(tidybayes)

library(dplyr)

library(ggplot2)

library(ggridges)

library(glue)

library(stringr)

library(forcats)

study.draws <- spread\_draws(m.brm, r\_Author[Author,], b\_Intercept) %>%

mutate(b\_Intercept = r\_Author + b\_Intercept, type = "Study-level Estimate")

pooled.effect.draws <- spread\_draws(m.brm, b\_Intercept) %>%

mutate(Author = "Pooled Effect", type = "Pooled Estimate")

fp\_data <- bind\_rows(study.draws, pooled.effect.draws) %>%

ungroup() %>%

mutate(b\_Intercept = b\_Intercept %>% exp) %>%

mutate(Author = str\_replace\_all(Author, "[.]", " ")) %>%

mutate(Author = reorder(Author, b\_Intercept))

#Create title and subtitles for the plot

main\_title <- "5-year stroke"

subtitle <- "non-informative prior"

#Plot

ggplot(data = fp\_data,

aes(y = relevel(Author, "Pooled Effect"),

x = b\_Intercept,

fill = type

)) +

#Add Density plots

geom\_density\_ridges(col = NA,

scale = 0.9, #Slightly decrease size so it fits

alpha = 0.7,

) +

geom\_vline(xintercept = 1, color = "black",

lwd = 1, linetype = 2) +

stat\_halfeye(alpha = 0.7, .width = 0.95) +

#Set colors

scale\_fill\_manual(values = c("salmon", "lightblue")) +

#Create title

ggtitle(main\_title,

subtitle = subtitle) +

#X and Y axes aesthetics

scale\_y\_discrete(name = "Study") +

scale\_x\_continuous(name = "Relative Risk",

trans = "log",

breaks = c(0.5, 1, 2)) +

#Set reasonable Y axis limits

coord\_cartesian(xlim = c(0.5, 2)) +

#Set theme

theme\_pubclean() +

theme(text = element\_text(size = 23),

plot.title=element\_text(face = "bold",hjust = 0.0, size = 18),

plot.subtitle = element\_text(face = "bold", size = 15, hjust = 0.0, color = "grey45"),

axis.text.x = element\_text(size = 20, face = "bold"),

axis.text.y = element\_text(size = 15, face = "bold"),

axis.title.x = element\_text(size = 25, face = "bold"),

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

axis.line = element\_line(colour = "black", linewidth = 1.2),

plot.margin = margin(0.5, 1, 0.5, 1, "cm"),

legend.background = element\_rect(fill = "transparent"),

legend.position = "none",

legend.text = element\_text(size = 12, face = "bold"),

legend.key.width = unit(1.5, "cm"),

legend.key.height = unit(0.75, "cm"))

**MYOCARDIAL INFARCTION**

PRIORS

priors <- c(prior(normal(0,2), class = Intercept),

prior(cauchy(0,0.5), class = sd))

META-ANALYSIS Log RR

m.brm <- brm(TE|se(seTE) ~ 1 + (1|Author),

data = mi,

prior = priors,

iter = 10000)

summary(m.brm)

pp\_check(m.brm)

ranef(m.brm)

post.samples <- posterior\_samples(m.brm, c("^b", "^sd"))

names(post.samples)

names(post.samples) <- c("logRR", "tau")

PLOT POSTERIOR DISTRIBUTION TE

ggplot(aes(x = logRR), data = post.samples) +

geom\_density(fill = "lightblue",

color = "lightblue", alpha = 0.7) +

geom\_point(y = 0,

x = mean(post.samples$logRR)) +

labs(x = expression(italic(logRR)),

y = element\_blank()) +

theme\_minimal()

PLOT POSTERIOR DISTRIBUTION TAU

ggplot(aes(x = tau), data = post.samples) +

geom\_density(fill = "lightgreen",

color = "lightgreen", alpha = 0.7) +

geom\_point(y = 0,

x = mean(post.samples$tau)) +

labs(x = expression(tau),

y = element\_blank()) +

theme\_minimal()

POSTERIOR DISTRIBUTION

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.1655)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.3075)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.4383)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.5481)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.5988)

library(tidybayes)

library(dplyr)

library(ggplot2)

library(ggridges)

library(glue)

library(stringr)

library(forcats)

study.draws <- spread\_draws(m.brm, r\_Author[Author,], b\_Intercept) %>%

mutate(b\_Intercept = r\_Author + b\_Intercept, type = "Study-level Estimate")

pooled.effect.draws <- spread\_draws(m.brm, b\_Intercept) %>%

mutate(Author = "Pooled Effect", type = "Pooled Estimate")

fp\_data <- bind\_rows(study.draws, pooled.effect.draws) %>%

ungroup() %>%

mutate(b\_Intercept = b\_Intercept %>% exp) %>%

mutate(Author = str\_replace\_all(Author, "[.]", " ")) %>%

mutate(Author = reorder(Author, b\_Intercept))

#Create title and subtitles for the plot

main\_title <- "5-year myocardial infarction"

subtitle <- "non-informative prior"

#Plot

ggplot(data = fp\_data,

aes(y = relevel(Author, "Pooled Effect"),

x = b\_Intercept,

fill = type

)) +

#Add Density plots

geom\_density\_ridges(col = NA,

scale = 0.9, #Slightly decrease size so it fits

alpha = 0.7,

) +

geom\_vline(xintercept = 1, color = "black",

lwd = 1, linetype = 2) +

stat\_halfeye(alpha = 0.7, .width = 0.95) +

#Set colors

scale\_fill\_manual(values = c("salmon", "lightblue")) +

#Create title

ggtitle(main\_title,

subtitle = subtitle) +

#X and Y axes aesthetics

scale\_y\_discrete(name = "Study") +

scale\_x\_continuous(name = "Relative Risk",

trans = "log",

breaks = c(0.5, 1, 2,3,4)) +

#Set reasonable Y axis limits

coord\_cartesian(xlim = c(0.5, 4)) +

#Set theme

theme\_pubclean() +

theme(text = element\_text(size = 23),

plot.title=element\_text(face = "bold",hjust = 0.0, size = 18),

plot.subtitle = element\_text(face = "bold", size = 15, hjust = 0.0, color = "grey45"),

axis.text.x = element\_text(size = 20, face = "bold"),

axis.text.y = element\_text(size = 15, face = "bold"),

axis.title.x = element\_text(size = 25, face = "bold"),

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

axis.line = element\_line(colour = "black", linewidth = 1.2),

plot.margin = margin(0.5, 1, 0.5, 1, "cm"),

legend.background = element\_rect(fill = "transparent"),

legend.position = "none",

legend.text = element\_text(size = 12, face = "bold"),

legend.key.width = unit(1.5, "cm"),

legend.key.height = unit(0.75, "cm"))

**REPEAT REVASCULARIZATION**

PRIORS

priors <- c(prior(normal(0,2), class = Intercept),

prior(cauchy(0,0.5), class = sd))

META-ANALYSIS Log RR

m.brm <- brm(TE|se(seTE) ~ 1 + (1|Author),

data = revasc,

prior = priors,

iter = 10000)

summary(m.brm)

pp\_check(m.brm)

ranef(m.brm)

post.samples <- posterior\_samples(m.brm, c("^b", "^sd"))

names(post.samples)

names(post.samples) <- c("logRR", "tau")

PLOT POSTERIOR DISTRIBUTION TE

ggplot(aes(x = logRR), data = post.samples) +

geom\_density(fill = "lightblue",

color = "lightblue", alpha = 0.7) +

geom\_point(y = 0,

x = mean(post.samples$logRR)) +

labs(x = expression(italic(logRR)),

y = element\_blank()) +

theme\_minimal()

PLOT POSTERIOR DISTRIBUTION TAU

ggplot(aes(x = tau), data = post.samples) +

geom\_density(fill = "lightgreen",

color = "lightgreen", alpha = 0.7) +

geom\_point(y = 0,

x = mean(post.samples$tau)) +

labs(x = expression(tau),

y = element\_blank()) +

theme\_minimal()

POSTERIOR DISTRIBUTION

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.0862)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.1740)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.2469)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.3221)

smd.ecdf <- ecdf(post.samples$logRR)

smd.ecdf(0.3853)

library(tidybayes)

library(dplyr)

library(ggplot2)

library(ggridges)

library(glue)

library(stringr)

library(forcats)

study.draws <- spread\_draws(m.brm, r\_Author[Author,], b\_Intercept) %>%

mutate(b\_Intercept = r\_Author + b\_Intercept, type = "Study-level Estimate")

pooled.effect.draws <- spread\_draws(m.brm, b\_Intercept) %>%

mutate(Author = "Pooled Effect", type = "Pooled Estimate")

fp\_data <- bind\_rows(study.draws, pooled.effect.draws) %>%

ungroup() %>%

mutate(b\_Intercept = b\_Intercept %>% exp) %>%

mutate(Author = str\_replace\_all(Author, "[.]", " ")) %>%

mutate(Author = reorder(Author, b\_Intercept))

#Create title and subtitles for the plot

main\_title <- "5-year repeat revascularization"

subtitle <- "non-informative prior"

#Plot

ggplot(data = fp\_data,

aes(y = relevel(Author, "Pooled Effect"),

x = b\_Intercept,

fill = type

)) +

#Add Density plots

geom\_density\_ridges(col = NA,

scale = 0.9, #Slightly decrease size so it fits

alpha = 0.7,

) +

geom\_vline(xintercept = 1, color = "black",

lwd = 1, linetype = 2) +

stat\_halfeye(alpha = 0.7, .width = 0.95) +

#Set colors

scale\_fill\_manual(values = c("salmon", "lightblue")) +

#Create title

ggtitle(main\_title,

subtitle = subtitle) +

#X and Y axes aesthetics

scale\_y\_discrete(name = "Study") +

scale\_x\_continuous(name = "Relative Risk",

trans = "log",

breaks = c(0.5, 1, 2,3)) +

#Set reasonable Y axis limits

coord\_cartesian(xlim = c(0.5, 3)) +

#Set theme

theme\_pubclean() +

theme(text = element\_text(size = 23),

plot.title=element\_text(face = "bold",hjust = 0.0, size = 18),

plot.subtitle = element\_text(face = "bold", size = 15, hjust = 0.0, color = "grey45"),

axis.text.x = element\_text(size = 20, face = "bold"),

axis.text.y = element\_text(size = 15, face = "bold"),

axis.title.x = element\_text(size = 25, face = "bold"),

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

axis.line = element\_line(colour = "black", linewidth = 1.2),

plot.margin = margin(0.5, 1, 0.5, 1, "cm"),

legend.background = element\_rect(fill = "transparent"),

legend.position = "none",

legend.text = element\_text(size = 12, face = "bold"),

legend.key.width = unit(1.5, "cm"),

legend.key.height = unit(0.75, "cm"))

**FREQUENTIST survival analysis**

library(survival)

library(rstpm2)

library(meta)

library(survminer)

**Kaplan Meier analysis for different timepoint**

fit <- survfit(Surv(time1, status) ~ treat, data = mort)

fit <- survfit(Surv(time1, status) ~ treat, data = stroke)

fit <- survfit(Surv(time1, status) ~ treat, data = mi)

fit <- survfit(Surv(time1, status) ~ treat, data = revasc)

**Hazard plot - mortality**

ggsurvplot(fit, data = mort, risk.table = TRUE, fun = "cumhaz", pval = FALSE, xlim = c(0,5), ylim = c(0,1), break.time.by = 1, censor = FALSE, conf.int = TRUE, palette = c("salmon", "light blue"), legend.title = "Treatment", legend.labs = c("PCI", "CABG"), break.x.by = 1, break.y.by = 0.1, xlab = "Time in years", fontsize = 4, risk.table.height = 0.35, font.main = c(15, "bold"), font.legend = c(12, "bold"))

ggsurvplot(fit, data = mort, risk.table = TRUE, fun = "cumhaz", pval = FALSE, xlim = c(0,5), ylim = c(0,0.22), break.time.by = 1, censor = FALSE, conf.int = TRUE, palette = c("salmon", "light blue"), legend.title = "Treatment", legend.labs = c("PCI", "CABG"), break.x.by = 1, break.y.by = 0.05, xlab = "Time in years", fontsize = 4, risk.table.height = 0.35, font.main = c(15, "bold"), font.legend = c(12, "bold"))

**Hazard plot - stroke**

ggsurvplot(fit, data = mort, risk.table = TRUE, fun = "cumhaz", pval = FALSE, xlim = c(0,5), ylim = c(0,1), break.time.by = 1, censor = FALSE, conf.int = TRUE, palette = c("salmon", "light blue"), legend.title = "Treatment", legend.labs = c("PCI", "CABG"), break.x.by = 1, break.y.by = 0.1, xlab = "Time in years", fontsize = 4, risk.table.height = 0.35, font.main = c(15, "bold"), font.legend = c(12, "bold"))

ggsurvplot(fit, data = mort, risk.table = TRUE, fun = "cumhaz", pval = FALSE, xlim = c(0,5), ylim = c(0,0.22), break.time.by = 1, censor = FALSE, conf.int = TRUE, palette = c("salmon", "light blue"), legend.title = "Treatment", legend.labs = c("PCI", "CABG"), break.x.by = 1, break.y.by = 0.05, xlab = "Time in years", fontsize = 4, risk.table.height = 0.35, font.main = c(15, "bold"), font.legend = c(12, "bold"))

**Hazard plot - myocardial infarction**

ggsurvplot(fit, data = mort, risk.table = TRUE, fun = "cumhaz", pval = FALSE, xlim = c(0,5), ylim = c(0,1), break.time.by = 1, censor = FALSE, conf.int = TRUE, palette = c("salmon", "light blue"), legend.title = "Treatment", legend.labs = c("PCI", "CABG"), break.x.by = 1, break.y.by = 0.1, xlab = "Time in years", fontsize = 4, risk.table.height = 0.35, font.main = c(15, "bold"), font.legend = c(12, "bold"))

ggsurvplot(fit, data = mort, risk.table = TRUE, fun = "cumhaz", pval = FALSE, xlim = c(0,5), ylim = c(0,0.22), break.time.by = 1, censor = FALSE, conf.int = TRUE, palette = c("salmon", "light blue"), legend.title = "Treatment", legend.labs = c("PCI", "CABG"), break.x.by = 1, break.y.by = 0.05, xlab = "Time in years", fontsize = 4, risk.table.height = 0.35, font.main = c(15, "bold"), font.legend = c(12, "bold"))

**Hazard plot - revascularization**

ggsurvplot(fit, data = mort, risk.table = TRUE, fun = "cumhaz", pval = FALSE, xlim = c(0,5), ylim = c(0,1), break.time.by = 1, censor = FALSE, conf.int = TRUE, palette = c("salmon", "light blue"), legend.title = "Treatment", legend.labs = c("PCI", "CABG"), break.x.by = 1, break.y.by = 0.1, xlab = "Time in years", fontsize = 4, risk.table.height = 0.35, font.main = c(15, "bold"), font.legend = c(12, "bold"))

ggsurvplot(fit, data = mort, risk.table = TRUE, fun = "cumhaz", pval = FALSE, xlim = c(0,5), ylim = c(0,0.2), break.time.by = 1, censor = FALSE, conf.int = TRUE, palette = c("salmon", "light blue"), legend.title = "Treatment", legend.labs = c("PCI", "CABG"), break.x.by = 1, break.y.by = 0.05, xlab = "Time in years", fontsize = 4, risk.table.height = 0.35, font.main = c(15, "bold"), font.legend = c(12, "bold"))

**BAYESIAN survival analysis**

library(rstanarm)

library(rstan)

library(survival)

library(bayesplot)

library(cowplot)

library(survRM2)

library(splines2)

fit.coxph <- coxph(Surv(time1, status) ~ treat, data = mort, x = TRUE)

summary(fit.coxph)

CHAINS <- 4

CORES <- 2

ITER <- 10000

SEED <- 42

prior.stan.const <- stan\_surv(

formula = Surv(time1, status) ~ arm,

data = revasc,

basehaz = "exp",

prior\_PD = TRUE,

chains = CHAINS,

cores = CORES,

iter = ITER,

seed = SEED)

prior.stan.const <- update(prior.stan.const, prior\_intercept = normal(0, 1), prior = normal(0, 0.5))

fit.stan.const <- update(prior.stan.const, prior\_PD = FALSE)

print(fit.stan.const, digits = 3)

**FREQUENTIST meta-analysis**

library(meta)

meta <- metabin(event.e=event.e, n.e=n.e, event.c=event.c, n.c=n.c, studlab=study, data=mortfreq, method = "Inverse", sm= "RR", random = TRUE, fixed = TRUE, method.bias = "Egger")

meta <- metabin(event.e=event.e, n.e=n.e, event.c=event.c, n.c=n.c, studlab=study, data=strokefreq, method = "Inverse", sm= "RR", random = TRUE, fixed = TRUE, method.bias = "Egger")

meta <- metabin(event.e=event.e, n.e=n.e, event.c=event.c, n.c=n.c, studlab=study, data=mifreq, method = "Inverse", sm= "RR", random = TRUE, fixed = TRUE, method.bias = "Egger")

meta <- metabin(event.e=event.e, n.e=n.e, event.c=event.c, n.c=n.c, studlab=study, data=revascfreq, method = "Inverse", sm= "RR", random = TRUE, fixed = TRUE, method.bias = "Egger")

forest(meta)