**R code for meta-analysis (R 4.4.1)**

**# 1. install R packages: metafor, mixmeta, dplyr, ggplot2, splines**

library(metafor)

library(mixmeta)

library(dplyr)

library(ggplot2)

library(splines)

**# 2. Data preparation**

**# Expected variables: study\_id, effect estimates (HR/RR/OR), lower\_CI, upper\_CI, and effect modifiers, including lifestyle factors (e.g., social\_engagement\_mean), follow-up duration (e.g., followup\_years), etc.**

dat <- read.csv("meta\_input.csv")

dat <- dat %>%

mutate(

yi = log(effect),

sei = (log(upper\_CI) - log(lower\_CI)) / (2 \* 1.96),

vi = sei^2

)

**# 3. Random-effects model (REML + HKSJ)**

res <- rma(yi, vi, data = dat, method = "REML", test = "knha", slab = study\_id)

summary(res)

exp(cbind(Estimate = coef(res), confint(res)))

**# 4. Heterogeneity (τ2, I2, and 95% predictive interval)**

tau2 <- res$tau2

I2 <- 100 \* tau2 / (tau2 + mean(dat$vi))

pred <- predict(res, transf = exp)

cat("τ² =", round(tau2,3), "; I² =", round(I2,1), "%\n")

cat("95% prediction interval (HR):", round(pred$pi.lb,3), "to", round(pred$pi.ub,3), "\n")

**# 5. Meta-regression with study-level moderators (primary research question: model lifestyle indicators). Example model: e.g., dat$social\_engagement\_mean**

if ("social\_engagement\_mean" %in% names(dat)) {

res\_mod <- rma(yi, vi, mods = ~ social\_engagement\_mean, data = dat,

method = "REML", test = "knha")

summary(res\_mod)

}

**# 6. Dose–response meta-analyses for continuous lifestyle variables, if data permits**

if (all(c("x","yi","vi","study\_id") %in% names(dat))) {

knots <- quantile(dat$x, probs = c(0.10, 0.5, 0.90), na.rm = TRUE)

Xs <- model.matrix(~ ns(x, knots = knots), data = dat)

mix\_spline <- mixmeta(y = yi, S = vi, X = Xs, id = study\_id,

data = dat, method = "reml")

summary(mix\_spline)

}

**# 7. Sensitivity analyses**

**# 7.1.Leave-one-out analysis.**

leave1out(res)

**# 7.2. Exclude studies that reported ORs or RRs.**

if ("measure\_type" %in% names(dat)) {

res\_HRonly <- rma(yi, vi, data = filter(dat, measure\_type == "HR"),

method = "REML", test = "knha")

cat("\nSensitivity Analysis: HR-only studies\n")

print(summary(res\_HRonly))

exp(cbind(Estimate = coef(res\_HRonly), confint(res\_HRonly)))

}

**# 7.3. Exclude studies with follow-up < 5 years.**

if ("followup\_years" %in% names(dat)) {

res\_longFU <- rma(yi, vi, data = filter(dat, followup\_years >= 5),

method = "REML", test = "knha")

cat("\nSensitivity Analysis: Follow-up ≥ 5 years\n")

print(summary(res\_longFU))

exp(cbind(Estimate = coef(res\_longFU), confint(res\_longFU)))

}

**# 7.4. Exclude studies at high risk of bias.**

if ("risk\_bias" %in% names(dat)) {

res\_lowROB <- rma(yi, vi, data = filter(dat, risk\_bias != "high"),

method = "REML", test = "knha")

cat("\nSensitivity Analysis: Excluding high risk of bias\n")

print(summary(res\_lowROB))

exp(cbind(Estimate = coef(res\_lowROB), confint(res\_lowROB)))

}

**# 8. Publication Bias**

funnel(res, xlab = "Log(HR)", main = "Funnel plot")

egger <- regtest(res, model = "rma") # Egger’s mixed-effects test

print(egger)

tf <- trimfill(res)

summary(tf)

funnel(tf, xlab = "Log(HR)", main = "Trim-and-fill funnel plot")

**# 9. Export Summary**

results\_summary <- data.frame(

k = res$k,

pooled\_logHR = coef(res),

pooled\_SE = res$se,

pooled\_HR = exp(coef(res)),

CI\_lower = exp(res$ci.lb),

CI\_upper = exp(res$ci.ub),

tau2 = tau2,

I2 = I2

)

write.csv(results\_summary, "meta\_results\_summary.csv", row.names = FALSE)