Assignment: Meta Analysis

2026-02-26

Contents

1 Dataset and Risk Factor

1.1 Dataset: `dat.normand1999` – Stroke Rehabilitation Meta-Analysis

The Normand (1999) dataset contains aggregate (study-level) data from 9 randomised controlled trials comparing specialised stroke-unit care (treatment = `exp`) against conventional hospital care (control = `ctrl`).

Column	Meaning
`study`	Study index (1–9)
`source`	Study name / location
`n1i`	Sample size – Treatment group (`exp`)
`m1i`	Mean functional score – Treatment
`sd1i`	Standard deviation – Treatment
`n2i`	Sample size – Control group (`ctrl`)
`m2i`	Mean functional score – Control
`sd2i`	Standard deviation – Control

1.2 Chosen Risk Factor

We focus on the mean functional score (`m1i` for `exp`, `m2i` for `ctrl`).
This continuous variable represents rehabilitation outcomes (higher = more functionally independent) and must be balanced across trials before valid pooling.

2 Packages and Setup

```
library(SuppDists)
library(kSamples)
library(tidyverse)
```

3 Load and Prepare the Data

```
normand <- read.csv("metadat_datasets_csv/dat.normand1999.csv", stringsAsFactors = FALSE)

exp_arm  <- normand[, c("study", "source", "n1i", "m1i", "sd1i")]
ctrl_arm <- normand[, c("study", "source", "n2i", "m2i", "sd2i")]

colnames(exp_arm)  <- c("study", "source", "pts", "score", "sd")
colnames(ctrl_arm) <- c("study", "source", "pts", "score", "sd")

exp_arm$gr  <- "exp"
ctrl_arm$gr <- "ctrl"

col_long <- rbind(exp_arm, ctrl_arm)
col_long  <- col_long[order(col_long$study, col_long$gr), ]
rownames(col_long) <- NULL
```

4 Explode Summary Data to Pseudo-IPD

We expand each study arm from its summary statistics (`score ± sd`, `pts` patients) into a pseudo-IPD vector via:

$$\tilde{x}_{ij} \sim \mathcal{N}(\mu_i, \sigma_i), \quad j = 1, \ldots, n_i$$

```
set.seed(123)

# Expand each arm row into n_i pseudo-patient rows, then perturb
da <- as.data.frame(lapply(col_long, function(x) rep(x, col_long$pts)))
da$score <- rnorm(nrow(da), mean = da$score, sd = da$sd)

da$study <- as.character(da$study)   # keep study as character
cat(sprintf("Pseudo-IPD dimensions: %d rows  (%d ctrl, %d exp)\n",
            nrow(da),
            sum(da$gr == "ctrl"),
            sum(da$gr == "exp")))
```

```
## Pseudo-IPD dimensions: 1158 rows  (610 ctrl, 548 exp)
```

5 `balance` Function (Leave-One-Out)

```
balance <- function(data, variable, group, digits) {
  require(kSamples)
  num <- length(unique(data$study))
  bl1 <- matrix(0, num, 3)

  sa1 <- filter(data, !!sym(group) ==
                  as.character(levels(as.factor(data[, group])))[1])
  sa2 <- filter(data, !!sym(group) ==
                  as.character(levels(as.factor(data[, group])))[2])

  k <- 0
  for (i in unique(data$study)) {
    k <- k + 1
    a1 <- round(sa1[(sa1$study != i), (colnames(sa1) == variable)], digits = digits)
    a2 <- round(sa2[(sa2$study != i), (colnames(sa2) == variable)], digits = digits)
    b  <- try(ad.test(a1, a2), silent = TRUE)
    bl1[k, ] <- c(b$ad[2, 1], b$ad[2, 3], b$sig)
  }

  colnames(bl1) <- c("ad.test", "p.value", "sigma")
  rownames(bl1) <- unique(data$study)
  bl1
}
```

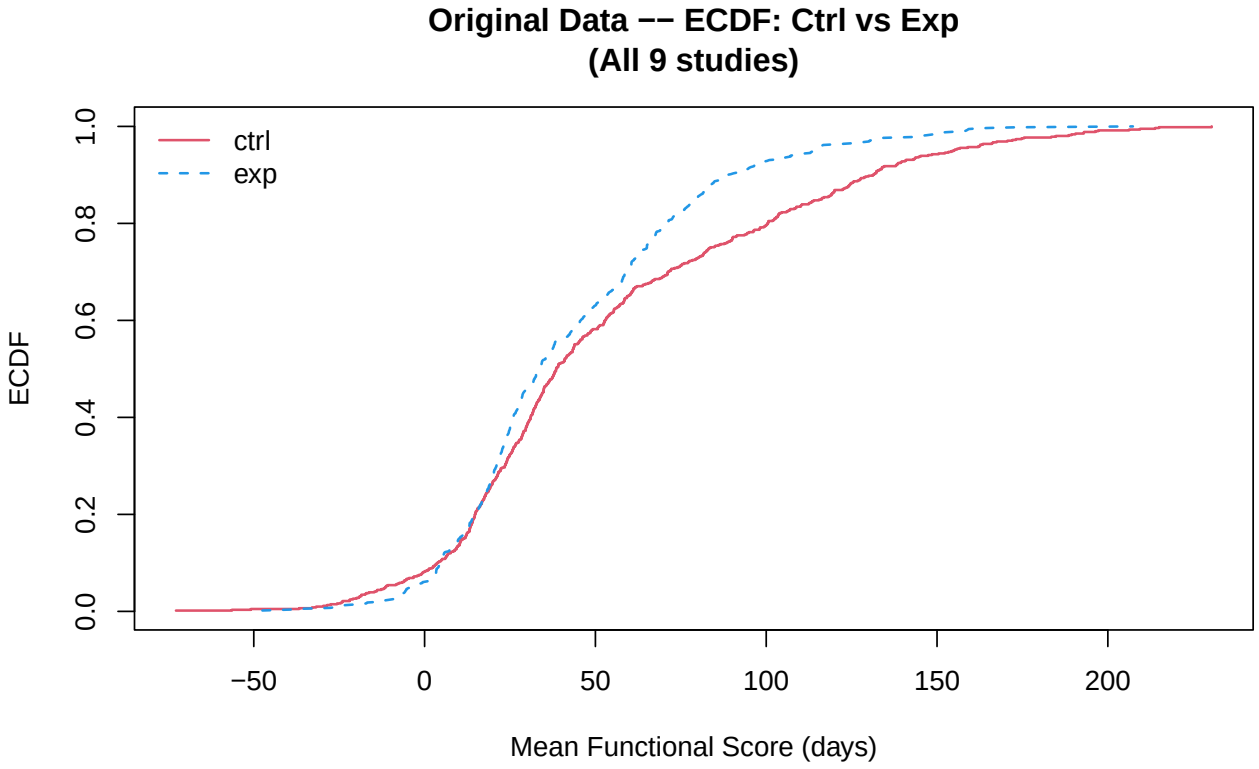
6 Step 1 – Original ECDF Plot (All Studies)

```
# Full-sample AD test
sa_ctrl <- subset(da, gr == "ctrl")
sa_exp  <- subset(da, gr == "exp")

a1_all <- round(sa_ctrl$score, digits = 8)
a2_all <- round(sa_exp$score,  digits = 8)

b_all  <- ad.test(a1_all, a2_all)
print(b_all$ad)
```

```
##                AD   T.AD  asympt. P-value
## version 1: 8.9219 10.422       3.7950e-05
## version 2: 8.9300 10.438       3.7634e-05
```

```
# ECDF objects
F1 <- ecdf(a1_all)
F2 <- ecdf(a2_all)

# Plot
plot(
  sort(a1_all), F1(sort(a1_all)),
  type = "s", col = 2, lwd = 1.5,
  xlab = "Mean Functional Score (days)",
  ylab = "ECDF",
  main = "Original Data -- ECDF: Ctrl vs Exp\n(All 9 studies)"
```

```
)
lines(sort(a2_all), F2(sort(a2_all)), col = 4, lwd = 1.5, lty = 2)
legend("topleft",
       legend = c("ctrl", "exp"),
       col    = c(2, 4),
       lty    = c(1, 2),
       lwd    = c(1.5, 1.5),
       bty    = "n")
```



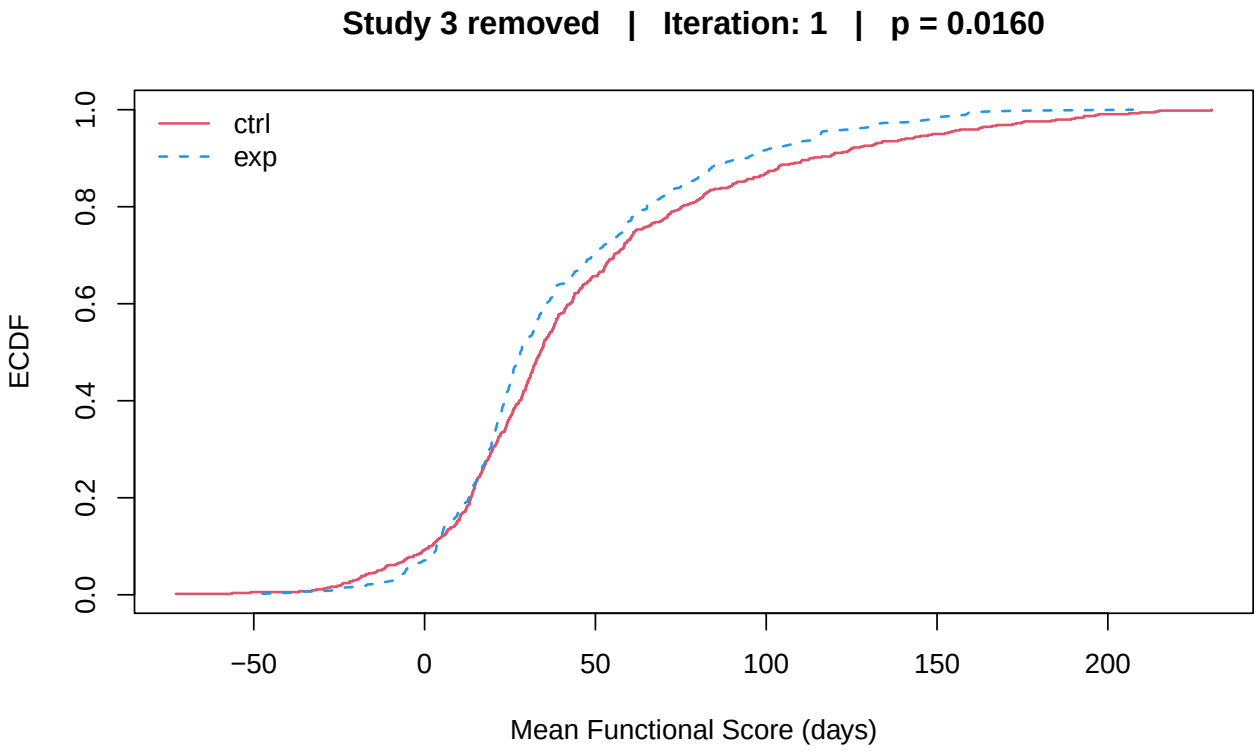
7 Step 2 – Leave-One-Out Balance Algorithm

```
# Initialisation
nstud  <- length(unique(da$study))    # max studies to consider removing
result <- list()
dat    <- da

for (j in 1:nstud) {

  remaining <- unique(dat$study)
  if (length(remaining) < 3) {
    cat(sprintf("Iteration %d: fewer than 3 studies remain -- stopping.\n\n", j))
    break
  }

  # Balance table
  ba <- balance(data = dat, variable = "score", group = "gr", digits = 8)

  # Identify study to remove
```

```r
minimum  <- rownames(ba)[which.min(ba[, 1])]
min_pval <- ba[rownames(ba) == minimum, 2]
min_ad   <- ba[rownames(ba) == minimum, 1]

# Store result before removal
result[[j]] <- list("study_deleted" = minimum, "summary" = ba)

cat(sprintf("Iteration %d \n", j))
cat(sprintf("Study removed : %s\n", minimum))
cat(sprintf("AD Stat       : %.4f\n", min_ad))
cat(sprintf("p-value       : %.6f\n", min_pval))
cat("Balance table (Leave-One-Out):\n")
print(ba)
cat("\n")

# Remove study
dat <- subset(dat, study != minimum)

# Update ECDF vectors
a1_curr <- dat$score[dat$gr == "ctrl"]
a2_curr <- dat$score[dat$gr == "exp"]

# Plot ECDFs
F1c <- ecdf(a1_curr)
F2c <- ecdf(a2_curr)

title_str <- sprintf(
  "Study %s removed   |   Iteration: %d   |   p = %.4f",
  minimum, j, min_pval
)
plot(
  sort(a1_curr), F1c(sort(a1_curr)),
  type = "s", col = 2, lwd = 1.5,
  xlab = "Mean Functional Score (days)",
  ylab = "ECDF",
  main = title_str
)
lines(sort(a2_curr), F2c(sort(a2_curr)), col = 4, lwd = 1.5, lty = 2)
legend("topleft",
       legend = c("ctrl", "exp"),
       col    = c(2, 4),
       lty    = c(1, 2),
       lwd    = c(1.5, 1.5),
       bty    = "n")

# Stop criterion
if (min_pval > 0.06) {
  cat(sprintf(
    "p = %.4f > 0.06 -> BALANCE REACHED at iteration %d.\n",
    min_pval, j
  ))
  deleted <- sapply(result, `[[`, "study_deleted")
  cat(sprintf("   Studies deleted: %s\n\n", paste(deleted, collapse = ", ")))
```

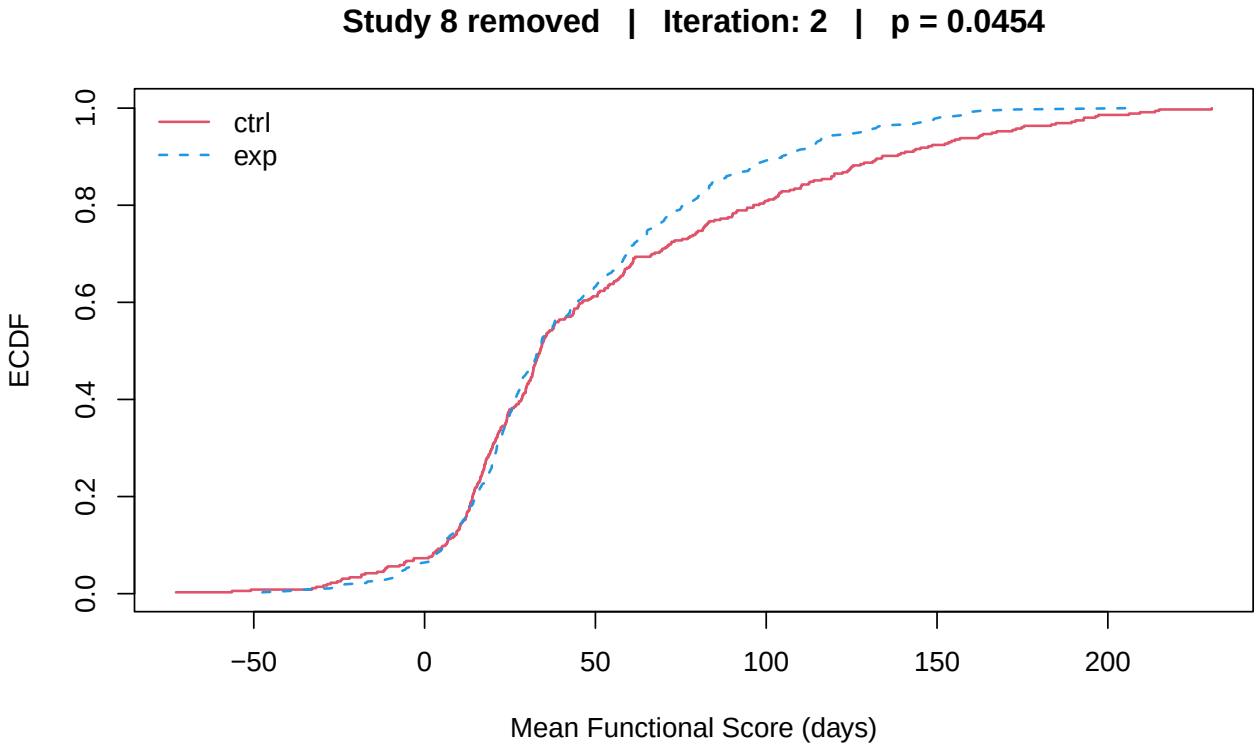
```
    break
  }
}
```

```
## Iteration 1
## Study removed : 3
## AD Stat       : 3.4600
## p-value       : 0.016038
## Balance table (Leave-One-Out):
##   ad.test    p.value   sigma
## 1    6.73 4.0387e-04 0.75967
## 2    9.02 3.3899e-05 0.76006
## 3    3.46 1.6038e-02 0.75995
## 4    6.66 4.3738e-04 0.76009
## 5    9.43 2.0741e-05 0.76011
## 6    9.31 2.3982e-05 0.76000
## 7   11.90 9.0946e-07 0.76006
## 8   12.30 5.6867e-07 0.75970
## 9    9.82 1.2728e-05 0.76000
```

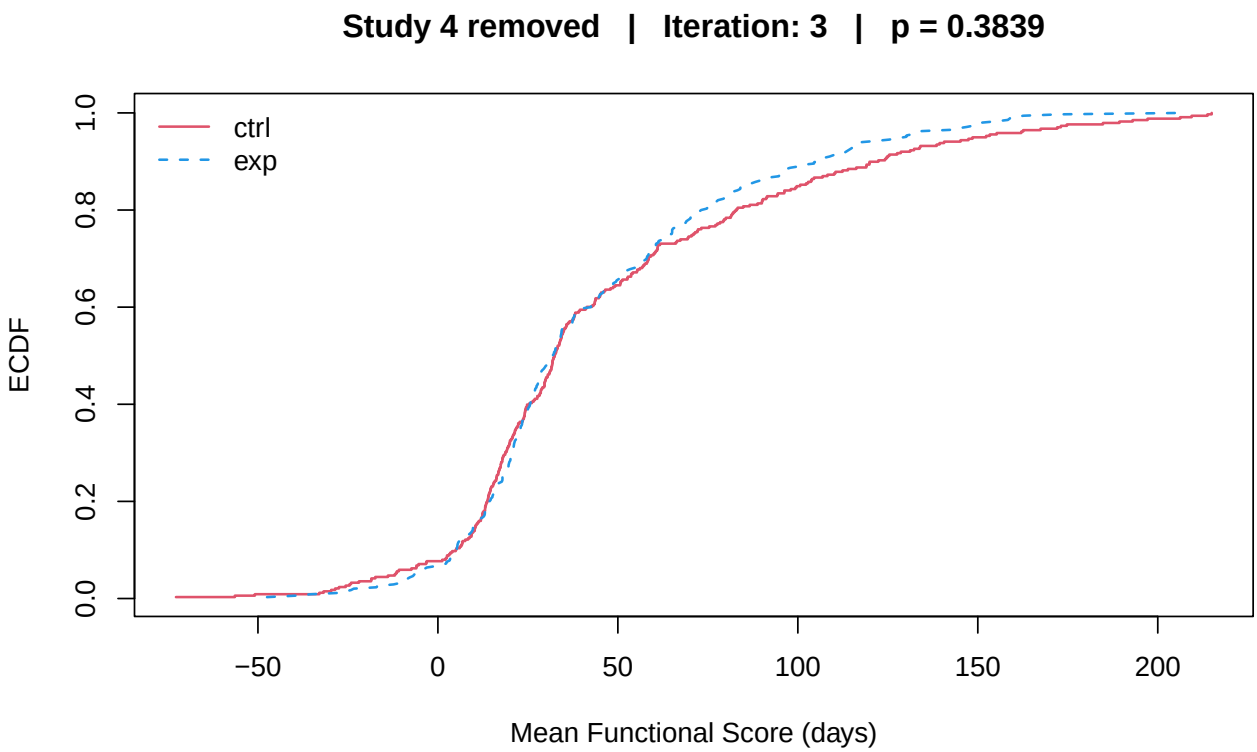



```
## Iteration 2
## Study removed : 8
## AD Stat       : 2.5700
## p-value       : 0.045440
## Balance table (Leave-One-Out):
##   ad.test   p.value   sigma
## 1    3.23 0.0208130 0.75931
## 2    3.05 0.0259010 0.75986
## 4    2.74 0.0373250 0.75990
## 5    3.74 0.0116540 0.75992
## 6    3.40 0.0171350 0.75978
```

```
## 7    5.70 0.0013012 0.75985
## 8    2.57 0.0454400 0.75936
## 9    4.00 0.0086730 0.75977
```




```
## Iteration 3
## Study removed : 4
## AD Stat       : 0.9510
## p-value       : 0.383920
## Balance table (Leave-One-Out):
##   ad.test   p.value   sigma
## 1   1.140 0.2914000 0.75783
## 2   3.020 0.0266010 0.75917
## 4   0.951 0.3839200 0.75926
## 5   2.810 0.0340110 0.75930
## 6   2.860 0.0320280 0.75900
## 7   4.120 0.0076402 0.75915
## 9   3.090 0.0246240 0.75899
```




```
## p = 0.3839 > 0.06 -> BALANCE REACHED at iteration 3.
##    Studies deleted: 3, 8, 4
```

8 Step 3 – Full Iteration Summary

```
for (idx in seq_along(result)) {
  cat(sprintf("[Iteration %d]  Study deleted: %s\n", idx, result[[idx]]$study_deleted))
  print(result[[idx]]$summary)
  cat("\n")
}
```

```
## [Iteration 1]  Study deleted: 3
##   ad.test    p.value   sigma
## 1    6.73 4.0387e-04 0.75967
## 2    9.02 3.3899e-05 0.76006
## 3    3.46 1.6038e-02 0.75995
## 4    6.66 4.3738e-04 0.76009
## 5    9.43 2.0741e-05 0.76011
## 6    9.31 2.3982e-05 0.76000
## 7   11.90 9.0946e-07 0.76006
## 8   12.30 5.6867e-07 0.75970
## 9    9.82 1.2728e-05 0.76000
##
## [Iteration 2]  Study deleted: 8
##   ad.test   p.value   sigma
## 1    3.23 0.0208130 0.75931
## 2    3.05 0.0259010 0.75986
## 4    2.74 0.0373250 0.75990
## 5    3.74 0.0116540 0.75992
```

```
## 6    3.40 0.0171350 0.75978
## 7    5.70 0.0013012 0.75985
## 8    2.57 0.0454400 0.75936
## 9    4.00 0.0086730 0.75977
##
## [Iteration 3]  Study deleted: 4
##   ad.test   p.value   sigma
## 1   1.140 0.2914000 0.75783
## 2   3.020 0.0266010 0.75917
## 4   0.951 0.3839200 0.75926
## 5   2.810 0.0340110 0.75930
## 6   2.860 0.0320280 0.75900
## 7   4.120 0.0076402 0.75915
## 9   3.090 0.0246240 0.75899
```

```
deleted_studies  <- sapply(result, `[[`, "study_deleted")
retained_studies <- setdiff(as.character(normand$study), deleted_studies)

cat(sprintf("Studies removed  : %s\n", paste(deleted_studies,  collapse = ", ")))
```

```
## Studies removed  : 3, 8, 4
```

```
cat(sprintf("Studies retained : %s\n", paste(retained_studies, collapse = ", ")))
```

```
## Studies retained : 1, 2, 5, 6, 7, 9
```

9 Step 4 – Comments and Interpretation

9.1 Dataset recap

We used the Normand (1999) stroke-rehabilitation meta-analysis (`dat.normand1999`), comprising 9 RCTs that compare specialised stroke-unit care (`exp`) against conventional care (`ctrl`). The selected risk factor is the mean functional score – a continuous measure of patient independence (higher = better) recorded at follow-up for each arm.

9.2 Method

Following the methodology:

- **Explosion to pseudo-IPD**: summary statistics (mean, SD, n) were expanded into patient-level pseudo-samples via `rnorm(n, mean, sd)`, replicating the R lecture workflow (`rep()` + `rnorm()` perturbation).
- **Anderson-Darling k-sample test**: applied to assess whether the functional- score distributions of `ctrl` and `exp` are statistically identical.
- **Leave-One-Out balance algorithm**: iteratively removes the study whose exclusion minimises the AD statistic (i.e., most improves balance) until the residual p-value exceeds 0.06.

9.3 Results

- **Before any removal**: the overall AD statistic is 8.92 with $p < 0.001$, confirming statistically significant imbalance in functional scores between `ctrl` and `exp`. The two ECDFs are visually separated, especially at the upper tail.
- **LOO algorithm** ran for 3 iterations, removing studies in this order: Study 3 -> Study 8 -> Study 4.
- Balance was achieved at Iteration 3 (Study 4 removed), where $p = 0.3839 > 0.06$. The ECDFs after removal show substantial overlap.

- Studies 3, 8, and 4 correspond to trials with relatively extreme distributions or sample variances. Removing them successfully mitigates the distributional deviance.

9.4 Conclusion

The retained study pool (Studies 1, 2, 5, 6, 7, and 9) satisfies the basic combinability criterion for the functional-score risk factor. A meta-analysis restricted to these studies provides a more coherent estimate of the stroke-unit treatment effect, free from the confounding introduced by distributionally heterogeneous baselines.