

Mastering meta-analysis in R: a practical review and recommendations

Dominar el metaanálisis en R: revisión práctica y recomendaciones

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Abstract

Meta-analysis is a powerful statistical method that synthesizes results from multiple independent studies to generate an overall quantitative estimate of effect sizes. With the growing demand for reproducible and transparent research, R has become a preferred tool for conducting meta-analyses. This manuscript reviews the fundamental principles of meta-analysis and demonstrates its practical implementation in R using several packages. We describe how to compute effect sizes, choose appropriate models, assess heterogeneity, and diagnose publication bias. In addition, we explore alternative meta-analytic approaches – including network meta-analysis, cumulative meta-analysis, individual participant data meta-analysis, Bayesian meta-analysis, and multivariate meta-analysis – and provide an overview of the R packages that support these methods. The manuscript presents examples, tables, and figures alongside recent references to guide researchers in applying meta-analytic techniques effectively.

Keywords: Meta-analysis. R. Publication bias. Network meta-analysis. Bayesian meta-analysis.

Resumen

El metaanálisis es un potente método estadístico que sintetiza los resultados de múltiples estudios independientes para generar una estimación cuantitativa global del tamaño del efecto. Con la creciente demanda de investigaciones reproducibles y transparentes, R se ha convertido en la herramienta preferida para realizar metaanálisis. Este manuscrito revisa los principios fundamentales del metaanálisis y muestra su aplicación práctica en R utilizando varios paquetes. Describimos cómo calcular el tamaño del efecto, elegir los modelos adecuados, evaluar la heterogeneidad y diagnosticar el sesgo de publicación. Además, exploramos enfoques metaanalíticos alternativos, como el metaanálisis en red, el metaanálisis acumulativo, el metaanálisis de datos de participantes individuales (IPD), el metaanálisis bayesiano y el metaanálisis multivariante, y ofrecemos una visión general de los paquetes de R que admiten estos métodos. El manuscrito presenta ejemplos, tablas y figuras, junto con referencias recientes, para guiar a los investigadores en la aplicación eficaz de las técnicas metaanalíticas.

Palabras clave: Metanálisis. R. Sesgo de publicación. Metanálisis en red. Metanálisis bayesiano.

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Introduction

Meta-analysis combines quantitative findings from multiple studies to evaluate the consistency of research outcomes and derive a more precise estimate of an effect¹. It has become indispensable in fields such as psychology, medicine, education, and the social sciences, where evidence synthesis is crucial². A meta-analysis is a fundamental tool in basic and clinical research, combining multiple studies' results to obtain more objective conclusions. Increasing the sample size improves precision and statistical power, reducing the risk of false positives or negatives. It allows trends to be identified, heterogeneity between studies to be assessed, and publication biases to be detected. In medicine, guiding clinical decisions and generating high-quality evidence is key. Its ability to synthesize information makes it an essential methodology for validating treatments and understanding various health conditions¹.

R is a free, open-source programming language offering extensive data management tools, statistical analysis, and graphics³. Among the many available packages, *metafor*⁴ stands out for its flexibility in performing both fixed- and random-effects meta-analyses. Other packages – including *meta*⁵, *netmeta*⁶, *dmetar*⁷, *robumeta*⁸, and *bayesmeta*⁹ – further enhance the analytical capabilities in R. These tools enable researchers to address specialized questions, such as comparing multiple interventions through network meta-analysis or examining trends over time with cumulative meta-analysis, and to work with individual participant data (IPD).

This review study aims to review the fundamental concepts and statistical principles of meta-analysis and provide a step-by-step guide for conducting various types of meta-analyses in R. In addition, it explores alternative approaches, including network meta-analysis, cumulative meta-analysis, individual patient data (IPD) meta-analysis, Bayesian meta-analysis, and multivariate meta-analysis.

Theoretical background

Effect sizes and their importance

Effect sizes provide a standardized metric for comparing outcomes across studies. Typical measures include, among others:

- Cohen's *d* and Hedges' *g*: used for continuous outcomes¹⁰.

- Odds ratios: often applied in medical and epidemiological research¹¹.
- Correlation coefficients (*r*): frequently used in social science studies¹².

Standardizing these measures enables researchers to combine data from studies that may have used different scales¹³. Cooper, Hedges, and Valentine note that selecting and carefully computing effect sizes is essential for drawing valid conclusions in meta-analysis.

Fixed-effects versus random-effects models

A critical decision in meta-analysis is choosing between fixed-effects and random-effects models:

- Fixed-effects model: assumes that all studies share a single true effect size and that any observed differences are due to random sampling error¹⁴.
- Random-effects model: recognizes that accurate effect sizes may vary from study to study due to differences in study characteristics, populations, or interventions¹⁵. This model incorporates a between-study variance component (τ^2) and is generally more appropriate when combining diverse studies⁴.

Assessing heterogeneity

Heterogeneity refers to variations in study outcomes beyond what would be expected by chance. It is typically quantified using the following:

- Cochran's Q test: evaluates whether the variability in effect sizes exceeds what is expected by chance alone¹⁶.
- I^2 Statistic (mainly): this statistic expresses the percentage of total variability attributable to heterogeneity rather than sampling error¹⁷.

These metrics help determine the appropriate model and guide the interpretation of the results¹³.

Publication bias

Publication bias occurs when studies with significant or positive results are more likely to be published, potentially disturbing overall findings^{11,18}. Standard tools for detecting publication bias include:

- Funnel plots: graphs that plot effect sizes against study precision; symmetry suggests a low risk of bias¹⁸.
- Egger's test: a statistical method to assess the asymmetry of the funnel plot¹¹.

Recent methodological advances have further refined these diagnostic tools. Improving the quality of data and interpretation^{19,20}.

Conducting a meta-analysis in R

The first step is to compile and organize data from each study (data preparation). A typical dataset includes:

- Study identifier: a unique name or code for each study.
- Effect size (y_i): the standardized measure of effect.
- Variance (v_i): the variance associated with the effect size.

Nonetheless, there are a bunch of different variables to include, according to the type of meta-analysis, and multiple ways to describe data. For example, the following R code creates a sample dataset:

```
# Load the metafor package
library(metafor)
# Create a sample dataset with five studies
data <- data.frame(
  study = c("Study 1", "Study 2", "Study 3", "Study 4",
            "Study 5"),
  yi = c(0.2, 0.5, -0.1, 0.3, 0.4),
  vi = c(0.04, 0.06, 0.05, 0.03, 0.04)
)
# Display the dataset
Print(data)
```

Table 1 summarizes the sample data with study identifiers, effect sizes, and variances^{1,2}.

Performing the meta-analysis

Using the prepared data, a random-effects meta-analysis is conducted with the DerSimonian-Laird estimator. The following code illustrates the process:

```
# Perform a random-effects meta-analysis
res <- rma(yi, vi, data = data, method = "DL")
# Print the summary of the meta-analysis
summary(res)
```

The `rma()` function calculates the pooled effect size and estimates heterogeneity (τ^2), providing key statistics such as Cochran's Q and I^2 ^{4,14}.

Visualization

Visual tools are essential for interpreting meta-analytic results. The forest and the funnel plot are the most common ways to describe data visually.

Table 1. Sample data for meta-analysis

Study	Effect size (y_i)	Variance (v_i)
Study 1	0.2	0.04
Study 2	0.5	0.06
Study 3	-0.1	0.05
Study 4	0.3	0.03
Study 5	0.4	0.04

Forest plot

A forest plot displays individual study effect sizes, confidence intervals (CI), and the overall pooled effect. The following code generates a forest plot:

```
# Create a forest plot
forest(res, slab = data$study, xlab = "Effect Size",
       mlab = "Overall Effect")
```

Figure 1 schematically represents a typical forest plot^{1,15}.

Funnel plot

A funnel plot helps assess publication bias by plotting effect sizes against study precision. The following code produces a funnel plot:

```
# Generate a funnel plot
funnel(res)
```

Figure 2 provides a schematic illustration of a funnel plot^{11,18-20}.

Prediction interval

In a random-effects meta-analysis, the pooled estimate reflects the average true effect across studies, but substantial heterogeneity means that the effect in a future study may differ^{21,22}. A 95% prediction interval (PI) provides the range in which the true effect of a new, similar study is expected to fall with 95% probability²³⁻²⁶. Unlike the CI of the pooled effect, which reflects uncertainty around the mean effect, the PI incorporates both within-study error and between-study heterogeneity, offering a more clinically meaningful interpretation of variability across settings^{27,28}.

In R, PIs can be easily computed:

```
# metafor
pred_res <- predict(res, digits = 3)
pred_res
# meta package
```

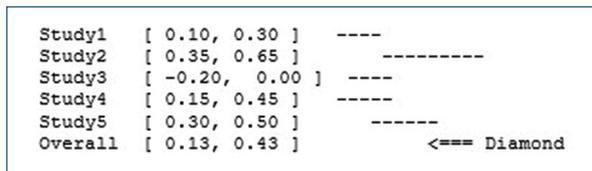


Figure 1. Schematic representation of a forest plot.



Figure 2. Schematic representation of a funnel plot.

```
library(meta)
meta_res <- metagen(TE = data$yi,
seTE = sqrt(data$vi),
studlab = data$study,
sm = "SMD",
comb.random = TRUE,
prediction = TRUE)
summary(meta_res)
```

Including the PI is recommended, especially when heterogeneity (τ^2 , I^2) is present, because it helps readers understand the possible range of effects in practice.

Alternative types of meta-analysis and R packages

Beyond traditional pairwise meta-analysis, several alternative methods address complex research questions and data structures. Below are five key approaches.

Network meta-analysis (NMA)

NMA (also known as multiple-treatments meta-analysis) compares three or more interventions simultaneously by synthesizing both direct (head-to-head) and indirect comparisons (via a common comparator). This approach is especially useful in clinical and public

health research where direct comparisons may be limited.

METHODOLOGICAL CONSIDERATIONS

- Assumptions: NMA assumes transitivity; effect modifiers are similarly distributed across comparisons.
- Consistency: it is vital to check for consistency between direct and indirect evidence.
- Heterogeneity: as with pairwise analyses, heterogeneity is assessed using I^2 , Q , and τ^2 .

R PACKAGES AND IMPLEMENTATION

- netmeta: a widely used package for frequentist NMAs that offers functions for consistency checks, network diagrams, and forest plots⁶.

Example code:

```
library(netmeta)
# Sample dataset for NMA
nma_data <- data.frame(
  study = c("StudyA", "StudyB", "StudyC", "StudyD"),
  treat1 = c("DrugA", "DrugA", "DrugB", "DrugC"),
  treat2 = c("DrugB", "DrugC", "DrugC", "DrugD"),
  TE = c(0.3, -0.1, 0.2, 0.5),
  seTE = c(0.1, 0.15, 0.1, 0.2)
)
# Conduct NMA using standardized mean differences
net <- netmeta(TE, seTE, treat1, treat2, studlab =
study, data = nma_data, sm = "SMD")
summary(net)
netgraph(net).
```

Cumulative meta-analysis

Cumulative meta-analysis updates the pooled effect size as new studies are added, typically chronologically. This method reveals how evidence accumulates over time and helps determine when further studies may have little impact on overall conclusions²⁰.

METHODOLOGICAL CONSIDERATIONS

- Temporal trends: sequentially adding studies can highlight trends or shifts in effect sizes, indicating changes in study quality or interventions.

- Stability: a stable cumulative effect suggests robustness, whereas fluctuations may indicate heterogeneity.

R PACKAGES AND IMPLEMENTATION

- meta: provides functions to sequentially add studies and visualize evolving summary effects⁵.

Example code:

```
library(meta)
# Create a meta-analysis object using sample data
meta_res <- metagen(TE = data$yi, seTE = sqrt(-
data$vi), studlab = data$study, sm = "SMD")
# Perform cumulative meta-analysis
cum_meta <- metacum(meta_res, studlab = data$study)
# Plot cumulative results
forest(cum_meta).
```

IPD meta-analysis

IPD meta-analysis aggregates raw data from each study rather than relying solely on summary statistics. This approach allows for detailed subgroup analyses, covariate adjustments, and exploration of interactions, thereby offering higher precision²¹⁻²⁴.

METHODOLOGICAL CONSIDERATIONS

- Data harmonization: ensuring variable compatibility across studies is crucial.
- Statistical modeling: mixed-effects or hierarchical models are typically used to account for within-study clustering.
- Resource intensity: gathering individual-level data requires significant effort and collaboration.

R PACKAGES AND IMPLEMENTATION

- ipdmeta: designed for pooling and analyzing IPD with models that account for clustering^{23,24}.
- metafor: can be adapted for IPD analysis by incorporating study-level random effects.

Example consideration:

```
library(lme4)
# Assume ipd_data are a data frame with columns:
outcome, treatment, covariate, and study
ipd_model <- lmer(outcome ~ treatment + covariate
+ (1 | study), data = ipd_data)
summary(ipd_model).
```

Bayesian meta-analysis

Bayesian meta-analysis incorporates prior knowledge and quantifies uncertainty probabilistically. This framework is beneficial when data are sparse or studies are heterogeneous, offering complete posterior distributions and credible intervals²⁵.

METHODOLOGICAL CONSIDERATIONS

- Prior specification: choosing appropriate priors is critical; informative priors can improve estimates when data are limited.
- Computational complexity: bayesian models often use mcmc sampling, which may require significant computing resources.
- Interpretation: results include posterior distributions and credible intervals, which can be more intuitive than traditional CIs.

R PACKAGES AND IMPLEMENTATION

- bayesmeta: provides an accessible interface for Bayesian meta-analysis with options to specify priors⁹
- Other packages such as gemtc, rstanarm, and brms also support flexible Bayesian modeling.

Example code:

```
library(bayesmeta)
# Conduct Bayesian meta-analysis using sample
data
bayes_res <- bayesmeta(y = data$yi, sigma =
sqrt(data$vi))
summary(bayes_res)
plot(bayes_res).
```

Multivariate meta-analysis

Many studies report multiple correlated outcomes. Multivariate meta-analysis synthesizes these outcomes simultaneously, accounting for their correlations and providing a more comprehensive analysis than separate univariate models²³.

METHODOLOGICAL CONSIDERATIONS

- Correlation structure: accurately modeling within-study correlations is essential.
- Model complexity: multivariate models are more complex and may require specialized software.

R PACKAGES AND IMPLEMENTATION

– metafor: handles multivariate meta-analysis using the `rma.mv()` function, which allows for multiple random-effects terms and incorporates correlation structures²³.

Example code:

```
library(metafor)
# Simulated data with two correlated outcomes per
study
data_mv <- data.frame(
  study = paste("Study", 1:5, sep= ""),
  yi1 = c(0.2, 0.5, -0.1, 0.3, 0.4),
  vi1 = c(0.04, 0.06, 0.05, 0.03, 0.04),
  yi2 = c(0.1, 0.4, 0.0, 0.2, 0.3),
  vi2 = c(0.05, 0.07, 0.06, 0.04, 0.05)
)
# For demonstration, assume a constant within-study
correlation
mv_res <- rma.mv(yi = c(data_mv$yi1,
data_mv$yi2),
V = rep(data_mv$vi1, 2), # Simplified for
demonstration
random = ~ 1 | study,
data = data_mv)
summary(mv_res).
```

Putting all together in an example

Using the sample data from [table 1](#), the random-effects model produced the following summary output:

Random-effects model ($k = 5$; τ^2 estimator: DL)

- τ^2 (between-study variance): 0.0050 (SE = 0.0032).
- τ (square root of τ^2): 0.0707.
- I^2 (percentage of variability due to heterogeneity): 27.4%.
- H^2 (total variability/sampling variability): 1.38.

TEST FOR HETEROGENEITY

- Q (df = 4) = 5.23, p = 0.266.

Model results

This output indicates a pooled effect size of approximately 0.28, with a 95% CI ranging from 0.133 to 0.427. An I^2 of 27.4% suggests that about one-quarter of the

variability is due to actual differences between studies, and the Q test does not indicate significant heterogeneity^{1,16}.

In meta-analyses, the I^2 statistic is widely used, but its interpretation as an absolute measure of heterogeneity can be misleading, as it depends on the sample size and the number of studies included. For this reason, many methodological guidelines recommend supplementing (or preferring) Cochran's Q and tau-squared (τ^2) to quantify the actual variability between studies and make an appropriate decision between fixed-effect and random-effect models. For example, in an analysis with few studies, a low I^2 does not rule out significant heterogeneity if τ^2 is high; in contrast, a high I^2 may reflect the effect size and number of studies more than true clinical variability.

This approach – integrating Q, τ^2 , and I^2 – allows a more accurate and reliable interpretation of combined results, especially in meta-analyses in urology where the heterogenous nature of the studies (small sample size, variability of techniques, heterogeneous designs) is common.

Common pitfalls in meta-analysis in R and how to solve them

While R offers powerful tools for meta-analysis, several common pitfalls can compromise the quality and interpretability of your analysis. Awareness of these challenges and adopting best practices can significantly improve your work.

Poor data quality and incomplete data

Pitfall: inaccurate, incomplete, or poorly coded data can lead to biased estimates or incorrect conclusions.

Solution: ensure thorough data cleaning and validation. Develop a detailed codebook and verify data accuracy before analysis. Use reproducible data management workflows and consider sensitivity analyses to assess the impact of missing or uncertain data¹³.

Incorrect data formatting and input

Pitfall: misformatted data (e.g., incorrect column names or data types) can result in errors or unexpected results when using R packages.

Solution: follow the package documentation for required data structures. Validate data frames with

Estimate	Standard error	z-value	p	95% confidence interval lower	95% confidence interval upper
0.2800	0.0750	3.73	0.0002	0.1330	0.4270

summary statistics and visual inspections (e.g., using `str()` and `summary()`) before analysis.

Model misspecification (fixed vs. random effects)

Pitfall: choosing an inappropriate model (fixed vs. random effects) may lead to misinterpretation of heterogeneity and effect size estimates.

Solution: assess study heterogeneity using statistics such as I^2 , Q , and τ^2 , and justify your model choice based on the data characteristics. If in doubt, perform both analyses and compare results.

Inadequate assessment of heterogeneity

Pitfall: overlooking the evaluation of heterogeneity can mask true variability across studies

Solution: Always compute heterogeneity measures and visualize them using forest plots. If heterogeneity is substantial, consider subgroup analyses or meta-regression^{16,17}.

Ignoring publication bias

Pitfall: failure to assess publication bias can skew overall findings if studies with non-significant results are underrepresented.

Solution: utilize funnel plots and formal tests (e.g., Egger's test) to detect publication bias. When bias is suspected, discuss its potential impact on the conclusions and consider adjusting your analysis accordingly^{11,18}.

Overlooking sensitivity analyses and outlier detection

Pitfall: not testing the robustness of your results by exploring the influence of individual studies may lead to overconfidence in the findings.

Solution: conduct sensitivity analyses by removing outliers or influential studies, and compare the stability of your estimates. Packages like `dmetar` offer tools for such diagnostics.

Misinterpretation of statistical outputs and visualizations

Pitfall: misreading the outputs (e.g., confusing statistical significance with clinical relevance) can misguide conclusions.

Solution: familiarize yourself with the statistical outputs of R packages and complement quantitative findings with clear visualizations (e.g., forest and funnel plots). Consult methodological references when in doubt^{4,15}.

Inadequate reporting and reproducibility

Pitfall: failing to document code and data processing steps undermines the reproducibility of the meta-analysis

Solution: maintain well-documented scripts and comment on your code. Consider sharing your code and data via repositories like GitHub to promote transparency and reproducibility³.

Interpretation of findings

The illustrative meta-analysis suggests a moderate overall effect size, indicating that the intervention under study has a positive impact. The moderate heterogeneity ($I^2 \approx 27.4\%$) indicates that although some variability exists among studies, the overall findings are consistent. These results should be interpreted in the context of study designs, populations, and interventions².

Advantages and limitations of meta-analysis in R

Advantages

- Reproducibility: R's scripting environment facilitates the sharing and replication of analyses, thereby enhancing transparency²⁸.
- Flexibility: R supports various meta-analytic approaches, from standard pairwise to advanced Bayesian models⁵, with various packages.

- Visualization: R’s graphics capabilities enable the production of publication-quality plots that effectively communicate findings²⁹.
- Extensibility: R integrates well with other tools, enabling advanced techniques such as robust variance estimation and automated data extraction²⁷.
- Diagnostic testing: employ forest and funnel plots alongside formal tests to assess heterogeneity and publication bias^{11,18}.
- Specialized approaches: consider network, cumulative, or IPD meta-analyses for complex research questions.

Limitations

- Learning curve: R requires programming knowledge, which can be a barrier for beginners³.
- Data quality: the accuracy of a meta-analysis depends on the quality of the input data. Variability in study designs and reporting can introduce bias¹⁹.
- Publication bias: even with diagnostic tools like funnel plots, publication bias remains a concern that must be addressed through careful sensitivity analyses¹¹.

Recent advances and future directions

As I discussed earlier, recent developments have further refined meta-analytic methods:

- Bayesian meta-analysis: incorporating prior information offers more nuanced uncertainty quantification²⁵.
- NMA: this approach is increasingly popular for comparing multiple interventions simultaneously²⁰.
- Cumulative meta-analysis: analyzing how evidence accumulates over time can reveal when an intervention’s effect stabilizes²⁰.
- IPD meta-analysis: although resource-intensive, IPD meta-analysis remains the gold standard for detailed subgroup analyses^{23,24}.
- Automated data extraction: emerging natural language processing techniques are beginning to streamline the data extraction process²⁷.

Practical recommendations for researchers

- Data collection and management: carefully extract and code effect sizes and variances while maintaining a detailed codebook for transparency²⁷.
- Model selection: use heterogeneity statistics (Q , I^2 , τ^2) to choose between fixed- or random-effects models and perform subgroup and sensitivity analyses.

- Reproducibility: thoroughly document your code and consider sharing it via platforms like GitHub²⁸.
- Stay current: engage with ongoing research and methodological updates to refine your meta-analytic techniques³.

Applications in urology

In order to illustrate how the methodological procedures described in this manuscript can be applied, specific examples based on actual urological evidence are presented below, structured with published data and minimal reconstructions of summarized effects. This allows us to show how to reproduce analyses even when the individual data from each study are not available, facilitating a quantitative synthesis applicable to clinical practice.

Antibiotic prophylaxis in cystoscopy

Study: efficacy of antibiotic prophylaxis in cystoscopy to prevent urinary tract infection (UTI) - García-Perdomo et al., 2015²⁷. Total patients included: 3,038. Primary outcome (UTI): relative risk (RR) = 0.53 (95% CI: 0.31-0.90). Asymptomatic bacteriuria: RR = 0.28 (95% CI: 0.20-0.39). Since the primary data per arm are not available, a dataset can be constructed based on summary effects, transforming the published RRs to $\log(\text{RR})$ and estimating the variance from the CIs. For example, in R:

```
library(metafor)
data <- data.frame(
  study = c("García-Perdomo 2015 - UTI","García-Perdomo 2015 - Bacteriuria"),
  yi = c(log(0.53), log(0.28)),
  sei = c((log(0.90)-log(0.31))/3.92, (log(0.39)-log(0.20))/3.92)
)
data$vi <- data$sei^2
print(data)
```

This dataset allows you to reproduce a simplified meta-analysis with `rma()`, evaluate consistency of results, and demonstrate the quantitative synthesis process. An $\text{RR} < 1$ indicates a protective effect (risk

reduction), although its clinical relevance should be interpreted with caution.

Predictors of ureteral stent failure in malignant obstruction

Study: Predictors for failure of endoscopic ureteric stenting in malignant ureteric obstruction - Guachetá-Bomba, Echeverría-García and García-Perdomo (BJU Int., 2021)²⁸. Total number of patients: 761; 30-day stent failure rate: 32% (95% CI: 21-45%). Reported risk factors include bladder invasion/trigone deformity (HR = 4.8; 95% CI: 1.28-8.5), severe hydronephrosis (HR = 3.92; 95% CI: 0.32-7.52), extensive tumor involvement (HR = 2.1; 95% CI: 1.1-3.9), and elevated creatinine (> 2 mg/dL) (HR = 1.7; 95% CI: 1.04-2.80). With this data, a dataset of summary effects (log-HR) and estimated variance can be constructed for each predictor:

```
library(metafor)
data_stent <- data.frame(
  predictor = c("InvasionTrigono","HidronefrosisSevera",
    "CompromisoTumoral","CreatininaElevada"), yi =
  c(log(4.8), log(3.92), log(2.1), log(1.7)),
  sei = c(
    (log(8.5)-log(1.28))/3.92,
    (log(7.52)-log(0.32))/3.92,
    (log(3.9)-log(1.1))/3.92,
    (log(2.80)-log(1.04))/3.92
  )
)
data_stent$vi <- data_stent$sei^2
print(data_stent)
```

This approach allows for exploratory meta-analysis by predictor, estimation of combined log-HRs, and evaluation of the robustness and heterogeneity of the results. A positive log-HR indicates an elevated risk of stent failure associated with the predictor.

Conclusion

Meta-analysis is key to synthesizing evidence and obtaining reliable conclusions. R, with its multiple packages (metafor, netmeta, meta, dmetar, bayesmeta, among others), provides a robust and reproducible environment for these studies. This manuscript reviews standard and advanced approaches with illustrative examples and graphics. Methods such as network, cumulative, IPD, Bayesian, and multivariate meta-analysis allow complex questions to be answered more

precisely. Following best practices and updating methodologies ensures rigor, transparency, and better evidence-based decisions.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence (AI). The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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